

History of Thoracic Anesthesiology

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Key Points

- Because of concern relating to the natural history of pneumothorax, the development of a thoracic surgery discipline comparatively was late.
- Tuberculosis was the stimulus to overcome concern and caution.
- Control of contaminating secretions was an early anesthesia objective.
- Rigid bronchoscopy, lung separation, and positive pressure ventilation are milestones of significance.
- Modern materials have enabled considerable advances in essentially early ideas.
- The anesthesia challenge of surgery of respiratory failure is to counteract the negative effects of positive pressure ventilation.
- Surgery for lung cancer remains the bulk of workload.

Introduction

Infantry in disciplined armies like those of the Romans were trained to inflict a penetrating stab injury to the chest wall. Early depictions capture the paradox of a small and bloodless injury inevitably being fatal: and a dignity to a transition into another world as deep to the wound the lung collapses, respiration becomes paradoxical, and carbon dioxide retention and hypoxia ease the passing. In the nineteenth century, as surgery was advancing apace because of antisepsis and anesthesiology, it

was opined that the surgeon's knife would for these old reasons inevitably lead to the death of the patient: surgically attempting to incise into the thorax was something of a taboo, only to be breached by *Ferdinand Sauerbruch* (1875–1951) little more than a century ago (Fig. 1.1).

The late beginning to the thoracic surgery discipline is overlooked. The author occasionally assisted the distinguished *Phillip Ayre* (1902–1979) who had worked with a surgical collaborator of Sauerbruch. This was *Laurence O'Shaugnessy* (1900–1940). A casualty of the Second World War, he left to posterity one of the earliest surgical methods of treatment for angina, and distinctive forceps that graced thoracic surgical instrument trays for 60 years and has been modified for minimal access use (Fig. 1.2).

The fatal process – wound, pleural penetration, lung collapse, respiratory, and cardiac arrest – was interrupted with construction of an operating environment that counteracted the elastic force that paralyses respiratory function. With encasement of the surgeon and patients' torso in a negative pressure chamber, atmospheric pressure (now positive in physiological terms) operated at the patient's exposed mouth and prevented the lung collapsing as soon as parietal pleura was breeched. Expired tidal ventilation and gas exchange can continue to counter the toxic effect, described as “pendeluft,” of moving physiological dead space gas back and forth between the lungs. Accumulation of carbon dioxide in the self-ventilating patients was delayed and albeit limiting operating time was enough to open the historical account of thoracic surgery.

FIG. 1.1. A diagram of Sauerbruch's negative-pressure chamber for thoracic anesthesia. The animal or patient's torso and the surgeons were enclosed in an airtight chamber evacuated to $-10\text{ cm H}_2\text{O}$ pressure. The subject was the anesthetized breathing air-ether spontaneously from a mask. When the thorax was opened the lung did not collapse and hypoxemia was averted, although hypercarbia would gradually develop due to pendeluft. This marked the beginnings of elective thoracic anesthesia and surgery. (From Mushin W, Rendell-Baker L. The origins of thoracic anaesthesia. Park Ridge, IL: The Wood Library-Museum; 1953. With permission The Wood Library-Museum, Park Ridge, IL.).

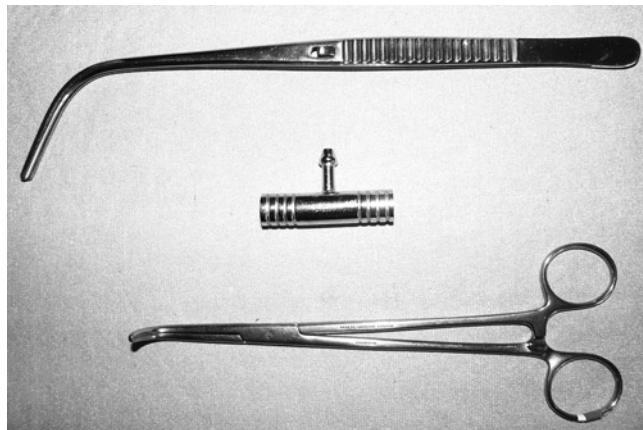
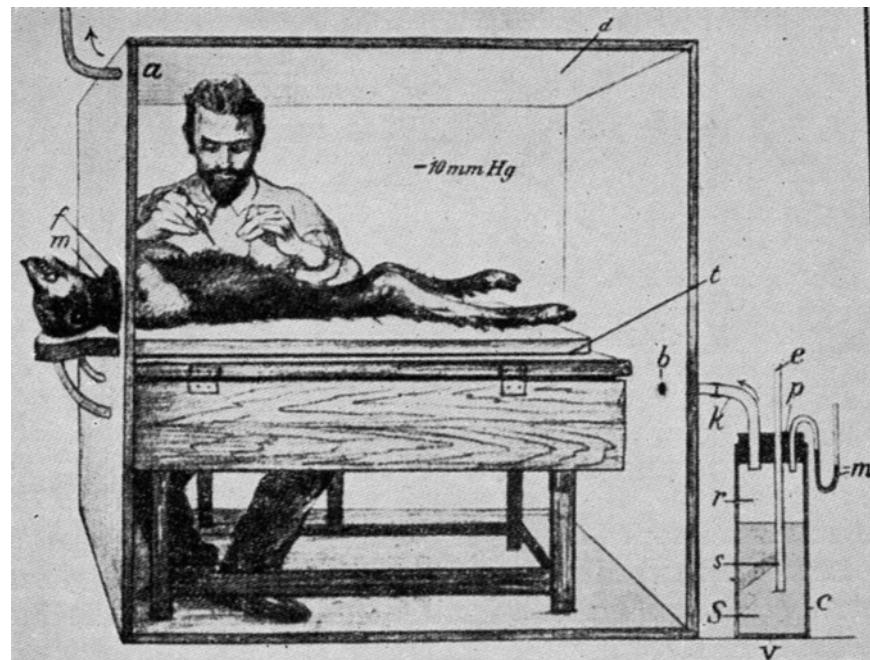


FIG. 1.2. Thoracic ephemera. From top to bottom: Krause's Forceps, Ayres "T" piece, O'Shaughnessy Forceps.

The Sauerbruch technique was replaced by more efficient methods to reverse intrapleural dynamics and based on supr atmospherical pressures applied to the airway – a move recognizable in modern day practices of tracheal intubation and positive pressure ventilation. The change is typical of an early phenomenon: the thoracic discipline attracted inspired minds, with ingenious ideas to build on templates of pioneers. Here are to be found stories of great physiologists, physicians, surgeons, and anesthesiologists without whom, for instance, the groundwork for a diversification into cardiac surgery would have been significantly delayed. Indeed in many countries, the latter services still are rooted in establishments that once were sanatoriums, serving the needs of early patients for chest surgery.

In each development, an anesthesiologist of the day has had to innovate, adapt, and change with new ideas, materials, and advances being presented to him or her. A formative

beginning with candle power disappeared with antimicrobial therapy but leaves a legacy of thoracoscopy, lateral thoractomy, lung separators, and pain relief techniques that are but little modified.

Paradigm shifts are usually marked by the two World Wars of the twentieth century. Though these are defining elements of any historical analysis, and certainly colored the individuals who are part of the story, developments in thoracic surgery that now govern modern practice are better seen in the light of changes in the medical challenges of disease which changed coincidentally at the same time points.

Ages of Thoracic Surgery

Surgery for Infective Lung Disease

The nineteenth century, a time of great population and societal movement particularly in and from Europe, was blighted by the "White Plague" (tuberculosis); an indiscriminate killer – irrespective of class, wealth, national boundaries, and unstoppable, a foreshadowing of AIDS: a heroine in the throes of consumption, a last hemoptysis, death – stuff of opera. Into this hopelessness strides the surgeon to deal with pulmonary cavities, septic foci, decayed and destroyed lung, bleeding points and copious, poisonous secretions that were more than capable of drowning the patient. Surgical repertoire after the Sauerbruch revelation was the artificial pneumothorax, empyema drainage, plombage (insertion of inert material into the thoracic cavity to promote lung collapse as therapy for tuberculosis), phrenic nerve crush, the thoracoplasty, and some tentative steps at resection – ordeals staged over days and weeks, but with an accrual of life-saving consequences for countless (Fig. 1.3).



FIG. 1.3. Chest X-ray of a left-sided thoracoplasty, ribs of the upper left hemithorax have been resected to promote left upper lobe collapse for tuberculosis therapy.

With no mechanisms of control of secretions and an ever-present danger of respiratory failure, standards for anesthesiology were sedation with opiates, topical, regional, and field blockade with local anesthetics to preserve self-ventilation so that cough and the ability to clear the airway were not lost.

Operating position became important. That of Trendelenburg was most effective to ensure that secretions, blood, and lung detritus drained gravitationally and not into the nonoperated lung. But, in the cachectic and septic sufferer of pulmonary tuberculosis or bronchiectasis, adoption of such steep head-down postures could prove fatal. The prone and semi-prone positions were gentler and less compromising. Surgeons got used to operating and approaching the lung and its constituents through a posterior thoracotomy. This spawned the postero-lateral thoracotomy, once tracheal intubation techniques enabled alternative, nongravitational ways of dealing with the secretion problem. Lung, esophagus, and heart became grist to the thoracic surgical mill.

As the era closed, the anesthesiologist (and the dawn of the specialist was at hand) had an experience of nitrous oxide and several volatile agents other than ether, notably chloroform and cyclopropane. Insufflation techniques, tracheal intubation, and rudimentary bronchial blocking techniques, which required a skill in rigid bronchoscopy, were tools of the expert. Several were using assisted ventilation before the advent of muscle relaxants. Prototype endobronchial tubes, bronchial blockers, and early positive pressure ventilation techniques were in position for a new age – ushered in with curare.

There is no greater symbol of the transition than the pneumonectomy of the British King, *George VI (1895–1952)*. Operated on in 1951 – for lung cancer – by a surgeon (*C. Price Thomas*

(1893–1973)) who was credited with his own operation (sleeve resection) for tuberculosis: the anesthesiologist (*Dr R. Machray*) had devised his own tracheal tube (but on the occasion used a Thompson bronchus blocker), wielded measured doses of diamorphine and pethidine, nitrous oxide, and the new agent, curare. And in the wings, spurred by intraoperative problems with ventilation, a trainee anesthesiologist (*William Pallister (1926–2008)*), was inspired to invent a new endobronchial tube specifically for the surgeon and his operation to avoid such critical incidents in the future. The surgeon later developed lung cancer for which he was operated on! The cigarette was yet to be seen as the cause and that this particular blight was largely man-made.

Surgery for Lung Cancer

Pulmonary resection for lung cancer came to dominate operating lists as the tuberculosis hazard receded to a point of rarity in developed countries with advances in public health that followed the Second World War. The favored method was general anesthesia with volatiles such as the new agent halothane, lung separation – commonly with double lumen tubes – muscle relaxants, and after the polio epidemics of the 1950s, positive-pressure ventilation with increasingly sophisticated ventilators. The Academic of the day, having acquired scientific tools, was beginning to recognize and investigate the subtle pathophysiological changes wrought by one-lung anesthesia.

In general, advances were defined by greater understanding of pulmonary physiology, limits and limitations of surgery particularly degree of resectability, and the fitness of patients to withstand ordeals of process, and more regard for quality of postresection existence. The crude practice of inserting a blocker through a rigid bronchoscope under topical anesthesia applied with Krause's Forceps, to test for the potential to survive a pulmonary resection, could be abandoned! Besides safeguarding the technological skills of an earlier era, the anesthesiologist needed to acquire a bedside expertise of the potential for respiratory failure to develop in a particular patient, based on simple pulmonary function tests (wet spirometry). In this era predating a foundation or philosophy for prolonged recovery with ventilator support and postoperative care resource, forecasting was on the basis that fatalities were theoretically due to carbon dioxide retention or right heart failure if excess lung was resected in reaching for a cure for a cancer: in practice sepsis and renal failure usually proved terminal.

The ending of this work pattern followed advances of plastics technology on equipment, fiberoptics on diagnostics and operating instruments, and computers on monitoring and performance. Surgery was moving into an age that had a patient demand to push operability beyond limits established for cancer. This desire was to be met with larger resource for intensive levels of postoperative care.

Although advances were truly innovative, these were fraught with risk. For a perspective on this, recall that pulse oximeters were experimental not universal, and end-tidal carbon dioxide

measurement nonexistent: operational decisions depended on blood gas monitoring with unsophisticated and slow automated systems, and the occasional use outside the laboratory of Swann-Ganz type pulmonary flotation catheters.

Surgery for Respiratory Failure

Defining elements include transplantation; but also revisits to treatment of emphysema (which had with chronic bronchitis reached significant proportions in developed countries); and technological and materials advances for trachea-bronchial disease which here-to-fore were off limits to all but a few establishments with special expertise and cardio-pulmonary bypass technology.

Orthotopic lung transplantation had been attempted in extremis (1963), but success in terms of long-term viability was not to be achieved for another 2 decades (1986). A new immuno-suppressant therapeutic era was to enable further, and this time successful efforts. Much of the credit goes to the Toronto group, under Dr Joel Cooper, whose selection and management templates resolved problems previously encountered by attempting to treat paraquat poisoning, routine use of corticosteroids for airways disease, tracheo-bronchial dehiscence, and reimplantation. Matching of lung preservation techniques to those for cardiac donors was a final step from experimental to mainstream and to the current healthy state of a thoracic organ transplant discipline.

Chronologically, not far behind, is lung volume reduction surgery, driven by many of the same innovators. Historically, this was just a revisit of old ideas and not a monumental surgical advance; but the lessons learnt were in particular for anesthesiology. In learning to deal with emphysema lung patho-physiology, a “down-side” of positive pressure ventilation was encountered with great frequency. The prevention and treatment of dynamic hyperinflation scenarios (“breath-stacking”) is now after a century, as big a challenge as that of “pendeluft” breathing was in its day.

Lung Separators

Three systems have evolved to facilitate one-lung ventilation: bronchus blocker, endobronchial tube, and double-lumen tube. The first two were of concept and had prototypes about the same time. Gale and Waters in 1931 have the credit for intubation of the contra-lateral bronchus prior to pneumonectomy: Crafoord and Magill as firsts for bronchial blocking. The double-lumen tube is a later development and as concept was taken from catheters, most notably the Carlens, devised for broncho-spirometric research, assessment, and investigation.

Devices were manufactured out of red-rubber and over the years many adaptations were made: right- and left-sided versions, carinal hooks, right upper lobe slots, extra inflatable cuffs: cuffs of red rubber, of latex rubber, and net-covered – to mention but a few.

The Blocker Story

It is to the particular genius of *Ivan Magill* (1888–1986) that the bronchus blocker is owed. With minor modifications it became a dominant technique for practitioners, use of which, as mentioned, had become a test for fitness for operation. Inserted through a rigid bronchoscope, the blocker could be placed accurately in the most complex of anatomical distortions wrought by tuberculosis. The state-of-the-art device was that of *Vernon Thompson* (1905–1995) (Fig. 1.4). However, endobronchial tube availability and the versatility of double lumen tubes meant that by the latter part of the twentieth century there were few but a dedicated band of practitioners with the skill to place and use blockers effectively and first choice status was lost. Plastics and fibreoptics led to reinvention for twenty-first century. “Univent,” Arndt, and Cohen systems following in quick succession as the concept was revitalized.

The Endobronchial Tube Story

These very obvious adaptations of tracheal tubes gave anesthesiologists a range of devices that served purpose for half a century. That of *Machray* was a long, single-cuffed tracheal tube and was placed in the left main bronchus under direct vision using an intubating bronchoscope as introducer (Fig. 1.5). Being able to mount these devices on a rigid scope, again a *Magill* credited idea, defined these tubes. The characteristic facilitated placement in the most distorted of airways, and allowed for ventilation through a wide-bore tube,

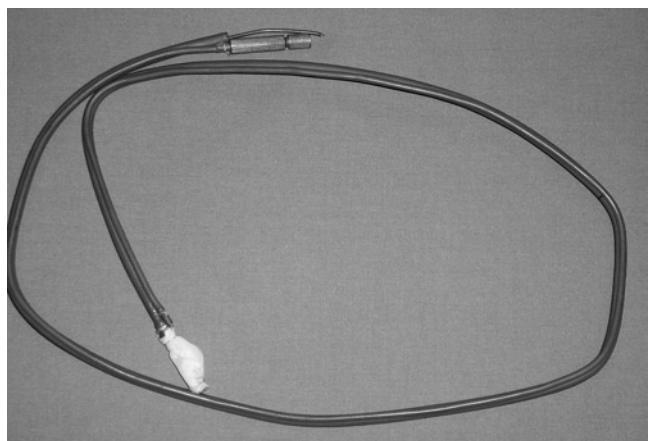


FIG. 1.4. Vernon Thompson bronchus blocker (circa 1943).



FIG. 1.5. Machray endobronchial tube and intubating bronchoscope.

bettered only by using a bronchus blocker outside and beside an endotracheal tube. Left sided Macintosh-Leatherdale and Brompton-Pallister; and the right-sided Gordon-Green were to prove the most enduring

The Double-Lumen Tube Story

Unlike the other types of lung separators, the double lumen tube was adapted and adopted rather than invented for the purpose of one-lung anesthesia and ventilation. The prototypes, notably that of *Eric Carlens* (1908–1990), were for physiological investigation. Models with the ventilation lumens positioned coaxially and anterior-posterior were tried but that of *Frank Robertshaw* (1918–1991) with its side-by-side lumens, anatomical shape, range of size, and low resistance characteristic dominated, to be later reproduced as plastic and disposable materials (e.g., Sheridan, Bronchocath) that replaced the increasingly unsuitable and anachronistic red rubber. The right-sided version was actually invented from a Gordon-Green endobronchial tube, the slot of which has remained the most effective device to ventilate the right upper lobe – an efficacy dependent on properties of red-rubber (Fig. 1.6).

Plastic and practice penetration by fiberoptic bronchoscopes of decreasing size and increasing sophistication and practicality led to much contemporary discussion about the “blind” placement of lung separators that replaced the tradition of rigid bronchoscopy as an aid to lung separation and bronchial cannulation.



FIG. 1.6. Tubes with right upper lobe ventilation slots: From left to right: Gordon-Green endobronchial, Robertshaw double lumen, Carlens (White model) double lumen, “Bronchocath” double lumen, and “Portex” prototype double lumen.

Though modern protocols are more fail-safe than reliance on clinical and observational skills, the modern didactic of medico-legality has trumped debate and stifled argument.

Origins of Thoracic Endoscopy

The ancient entertainment of sword swallowing had long demonstrated the feasibility of inserting rigid instruments into the esophagus. In 1895 a scope was first passed through a tracheotomy opening to be quickly followed by endoral attempts but at the limits of proximal lighting systems. *Chevalier Jackson* (1865–1958) was not the originator but he certainly was a pioneer and the first master of distal lighting systems, with a record on removal of foreign bodies that stands unsurpassed to this day (Fig. 1.7). To him are owed the rules that made the dangerous art of sword swallowing into a scientific tool

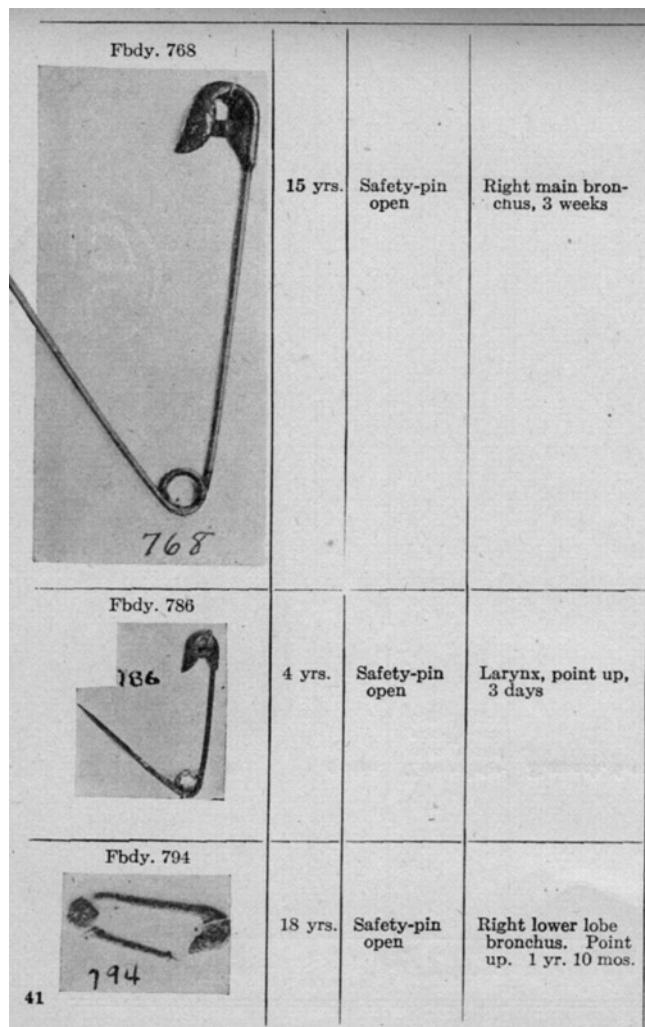


FIG. 1.7. A series of safety pins removed from the airway by rigid bronchoscopy (from Jackson C. Foreign bodies in air and food passages. Charted experience in cases from no. 631 to no. 1155 at the Bronchoscopic Clinic; 1923.).

for therapy and diagnosis both in the esophagus and in the tracheo-bronchial tree: and, the subtleties of neck positioning that ensure either the esophagus or trachea is cannulated: a whole philosophy of skill that has been negated by the flexible nature of modern tools.

Now the only indications for rigid bronchoscopy are foreign body removal and occasional stent insertion, but there was a time when rigid bronchoscopy was indispensable for operative assessment, bronchography, diagnostics, insertion of lung separators, postoperative lung toilet, and treatment of broncho-pleural fistula. Under careful local anesthetic application, topical, regional, and cricothyroid puncture, the technique could be conducted with such skill that no less an illustrious patient than *Geoffrey Organe* (1908–1989) the Professor of Anaesthesia, Westminster Hospital, London, was able to declare the experience as “more pleasant than going to the dentist.”

Trying to produce an artificial pneumothorax frequently failed because of adhesions. In 1913, a Swedish surgeon, Hans Christian Jacobeus, reported on the use of a modified cystoscope to look into the chest and used a second port for instruments, such as probes and cautery, to deal with recalcitrant adhesions. It is not hard to see how this concept has evolved.

Tracheobronchial Stenosis

As technological advance is on the brink of tracheal reconstruction using biological methods, it is important not to forget that this state has been reached by a long and hard struggle to overcome the challenge for surgery and healing inherent in innately poor mammalian vascular supply of the tracheobronchial tree. The era of tracheal resection and repair was to be dominated by *Hermes Grillo* (1923–2006), the Chief of Thoracic Surgery at the Massachusetts General Hospital. There was a brief period of tracheoplasty and silicon replacements, all of which were major anesthesiological undertakings but developments in stents, largely modeled on similar devices for esophageal stricture, had become prevalent at the end of the twentieth century. Solid-state devices of silicon were replaced by a range of self-expanding ones made of non-reactive and malleable materials such as nitinol which have resulted in less challenging anesthesia scenarios.

Esophageal Surgery

Originally, surgery on the esophagus was very much a development of chest surgery. Several medical cultures retained a linkage late into the twentieth century, but this was largely a technical connection because of commonality of anesthesiological requirements like lung isolation. Most countries have now broken the connection, and the esophagus is largely seen as outside the hegemony of thoracic practice. Cancer,

achalasia, and hiatus hernia, once part of the tougher end of the surgical diet, are now treated less traumatically and invasively.

As with pulmonary resection, early developments were based on totemic patients by small teams, whose successes and tribulations sustained knowledge that relief by surgical means ultimately was going to be of benefit to many more. A single case survivor of 13 years after transpleural esophagectomy by *Franz Torek* (1861–1938) in New York in 1913 was a beacon for 3 decades. The anesthetist was *Carl Eggers* (1879–1957) who administered ether through a woven silk tracheal tube to a self-ventilating patient. In 1941, the world experience of the technique was 17 survivors of 58 patients.

Pain Relief

Modern analgesics can be traced to the coca leaf, opium poppy, and willow bark but administration other than by ingestion or inhalation needed the hypodermic needle. Spinal injection (1898), intercostal nerve blockade (1906), paravertebral injection (1906), and extradural (1921) are the historical sequence for local anesthetic procedures of context.

Survivors of thoracoplasty operations tell of hearing their ribs being cracked as, in the later stages of the operation, the thoracic cage was rearranged: few attendants were prepared to risk general anesthesia. A specimen technique of Magill's for this operation, first performed in the UK by *Hugh Morriston Davies* (1879–1965) in 1912, included premedication with opiates, supraclavicular brachial plexus block, intercostal nerve block, dermal infiltration of skin incision site and towel clip points as well as subscapular infiltration and much titration of dilutions of adrenalin (epinephrine). *J Alfred Lee* (1906–1989) (author of the classic: *A Synopsis of Anaesthesia*, first produced in 1947) states advantages of local as opposed to general anesthesia: reduced risk of spread of disease, better elimination of secretions as cough reflex is not abolished, quicker convalescence because patient is less upset by drugs and needs less nursing care, and abolition of explosion risk.

Paravertebral blockade, first credited to Sellheim, went on to be used for operative pain relief, postthoracotomy neuralgia, and even angina and thoracic pain of unknown etiology. Subarachnoid block enjoyed a period in thoracic surgery, but the “high” nature meant that it was a hazardous technique because of uncontrolled hypotension and suppression of respiration. Epidural anesthesia was limited by the toxicity of agents, hazard of hemodynamic collapse, the short-lived nature of single-shot procedures, and logistics and feasibility of process in the context of hospital environment. Continuous analgesia perioperatively was only realistic with small-bore tubing and got impetus from the link to improved postoperative respiratory function.

Correlation of pain relief and reversal of some of the negative effects of surgery led to recognition that pain relief objectives could be broadened from humanitarian and reactive. A new philosophy has arisen: it is a proactive one to capitalize

on observations that pain relief techniques contribute to the healing process by promoting a sense of well-being, preserving gastrointestinal function, improving anastomotic blood flow, and facilitating management of comorbidity.

Conclusion

The impetus for surgical development and advance are all in context, and in none more than thoracic practice is this true: phases, even paradigm shifts, defined by disease, sociology and advances in knowledge, therapeutics and, in the case of anesthesiology, by drugs, materials and technology. As historical evolution, much of current practice is recognizable.

A modern age is already characterized by a circumspect use of volatile agents, but predictable forces of surgery are the demand for minimal access and the use of once-only disposable materials that have already seen the demise of much of local infrastructure to process sterile equipment and surgical hygiene. Hospital-acquired infection morbidity is a given, as are epidemics of asbestos-related pleural-pulmonary disease as this ubiquitous “pathogen” escapes from twentieth century confines. A new epidemic, obesity, will gain momentum.

Lung cancer treatment options show little sign of being bettered by other than surgical methods. Tuberculosis has a new drug-resistant guise. Could history repeat itself?

Further Reading

- Jackson C. Foreign bodies in the air and food passages. *Trans Am Laryngol Rhinol Otol Soc.* 1923.
- Sellors TH. *Surgery of the thorax*. London: Constable; 1933.
- Jackson C, Jackson CL. *Bronchoesophagology*. WB Saunders: Philadelphia, PA; 1950.
- Mushin WW, Rendell-Baker L, editors. *The principles of thoracic anaesthesia: past and present*. Oxford: Blackwell Scientific; 1953.
- Lee JA. Anaesthesia for thoracic surgery. In: *A synopsis of anaesthesia*. 3rd ed. Bristol: John Wright; 1955. p. 386–402.
- Mushin WW, editor. *Thoracic anaesthesia*. Philadelphia, PA: FA Davis; 1963.
- Hurt R. *The history of cardiothoracic surgery from early times*. New York, NY: Parthenon; 1996.
- Ellis H. The pneumonectomy of George VI. In: *Operations that made history*. London: Greenwich Medical Media; 1996. p. 123–30.
- Maltby JR, editor. *Notable names in anaesthesia*. London: Royal Society of Medicine; 1998.

Preanesthetic Assessment for Thoracic Surgery

Peter Slinger and Gail Darling

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Key Points

- All patients having pulmonary resections should have a preoperative assessment of their respiratory function in three areas: lung mechanical function, pulmonary parenchymal function, and cardiopulmonary reserve (the “three-legged stool” of respiratory assessment).
- Following pulmonary resection surgery, it is usually possible to wean and extubate patients with adequate predicted post-operative respiratory function in the operating room provided they are “AWaC” (alert, warm and comfortable).
- Preoperative investigation and therapy of patients with coronary artery disease for noncardiac thoracic surgery is becoming a complex issue. An individualized strategy in consultation with the surgeon, cardiologist, and patient is required. Myocardial perfusion, CT coronary angiography, and other advances in imaging are used increasingly in these patients.

- Geriatric patients are at a high risk for cardiac complications, particularly arrhythmias, following large pulmonary resections. Preoperative exercise capacity is the best predictor of post-thoracotomy outcome in the elderly.
- In the assessment of patients with malignancies, the “four M’s” associated with cancer must be considered: mass effects, metabolic effects, metastases, and medications.
- Perioperative interventions which have been shown to decrease the incidence of respiratory complications in high-risk patients undergoing thoracic surgery include: cessation of smoking, physiotherapy, and thoracic epidural analgesia.

Introduction

Thoracic anesthesia encompasses a wide variety of diagnostic and therapeutic procedures involving the lungs, airways, and other intrathoracic structures. As the patient population

presenting for noncardiac thoracic surgery has changed, so have the anesthetic techniques required to manage these patients. Thoracic surgery at the beginning of the last century was primarily for infectious indications (lung abscess, bronchiectasis, empyema, etc.). Although these cases still present for surgery in the post-antibiotic era, now the commonest indications are related to malignancies (pulmonary, esophageal and mediastinal). In addition, the last two decades has seen the beginnings of surgical therapy for end-stage lung diseases with procedures such as lung transplantation and lung-volume reduction.

Recent advances in anesthetic management, surgical techniques, and perioperative care have expanded the envelope of patients now considered to be “operable” [1]. This chapter will focus primarily on preanesthetic assessment for pulmonary resection surgery in cancer patients. However the basic principles described apply to diagnostic procedures, other types of nonmalignant pulmonary resections and to other chest surgery. The major difference is that in patients with malignancy the risk/benefit ratio of canceling or delaying surgery pending other investigation/therapy is always complicated by the risk of further spread of cancer during any extended interval prior to resection. Cancer surgery is never completely “elective” surgery.

A patient with a “resectable” lung cancer has a disease that is still local or local-regional in scope and can be encompassed in a plausible surgical procedure. An “operable” patient is someone who can tolerate the proposed resection with acceptable risk. Anesthesiologists are not gate-keepers. Normally, it is not the anesthesiologist’s function to assess these patients to decide who is or is not an operative candidate. In the majority of situations, the anesthesiologist will be seeing the patient at the end of a referral chain from Chest or Family Physician to Surgeon. At each stage, there should have been a discussion of the risks and benefits of operation. It is the anesthesiologist’s responsibility to use the preoperative assessment to identify those patients at elevated risk and then to use that risk assessment to stratify perioperative management and focus resources on the high-risk patients to improve their outcome (Fig. 2.1). This is the primary function of the preanesthetic assessment. However, there are occasions when the anesthesiologist is asked to contribute his/her opinion whether a specific high-risk patient will tolerate a specific surgical procedure. This may occur preoperatively but also occurs intraoperatively when the surgical findings suggest that a planned procedure, such as a lobectomy, may require a larger resection such as a pneumonectomy. For these reasons it is imperative that the anesthesiologist have a complete preoperative knowledge of the patient’s medical status and also an appreciation of the pathophysiology of lung resection surgery. There has been a comparatively small volume of research on the short-term (<6 weeks) outcome of these patients. However, this research area is currently very active and there are several studies which can be used to guide anesthetic management in the perioperative period where it has an influence on outcome.

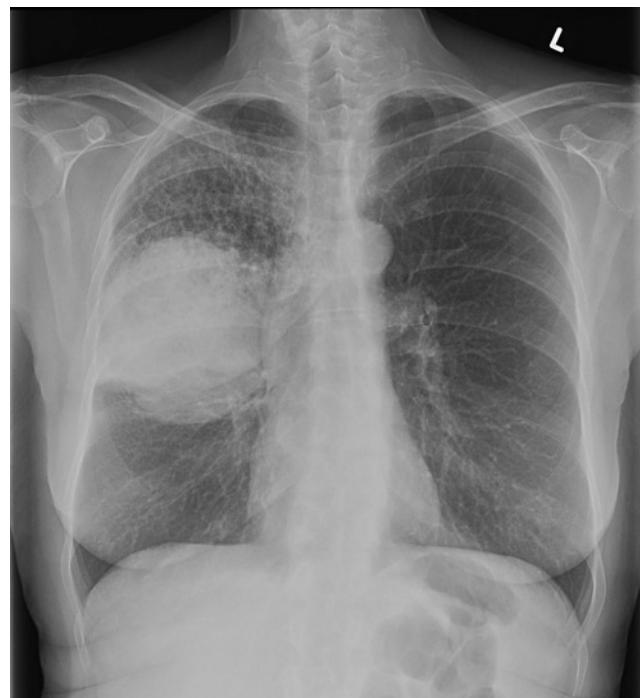


FIG. 2.1. Chest X-ray of a patient with a carcinoma of the right upper lobe scheduled for possible lobectomy or pneumonectomy. The purpose of the preoperative anesthetic assessment of this patient is to stratify the patient’s risk and to identify factors which can be managed to improve the perioperative outcome.

An increasing number of thoracic surgeons are now being trained to perform “lung-sparing” resections such as sleeve-lobectomies or segmentectomies and to perform resections with minimally invasive techniques such as video-assisted thoracoscopic surgery (VATS). The postoperative preservation of respiratory function has been shown to be proportional to the amount of functioning lung parenchyma preserved. To assess patients with limited pulmonary function, the anesthesiologist must appreciate these newer surgical options in addition to the conventional open lobectomy or pneumonectomy.

Pre-thoracotomy assessment naturally involves all of the factors of a complete anesthetic assessment: past history, allergies, medications, upper airway, etc. This chapter will concentrate on the additional information, beyond a standard anesthetic assessment, that the anesthesiologist needs to manage a thoracic surgical patient. Practice patterns in anesthesia have evolved such that a patient is commonly assessed initially in an outpatient clinic and often not by the member of the anesthesia staff who will actually administer the anesthesia. The actual contact with the responsible anesthesiologist may be only 10–15 min prior to induction. It is necessary to organize and standardize the approach to preoperative evaluation for these patients into two temporally disjoint phases: the initial (clinic) assessment and the final (day-of-admission) assessment. There are elements vital to each assessment which will be described.

Assessment of Respiratory Function

The major cause of perioperative morbidity and mortality in the thoracic surgical population is respiratory complications. Major respiratory complications such as: atelectasis, pneumonia, and respiratory failure occur in 15–20% of patients and account for the majority of the expected 3–4% mortality [2]. Cardiac complications such as: arrhythmia, ischemia, etc. occur in 10–15% of the thoracic population. Postoperative factors associated with a prolonged length of stay (>14 days) after lobectomy are listed in Table 2.1 [3]. The primary focus for the anesthesiologist is to assess the risk of postoperative pulmonary complications.

The best assessment of respiratory function comes from a detailed history of the patient's quality of life. All pulmonary resection patients should have baseline simple spirometry preoperatively to measure forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) (Fig. 2.2) [4]. Simple portable spirometers are available that can be used easily in the clinic or at the bedside to make these measurements (Fig. 2.3). Objective measures of pulmonary function are required to guide anesthetic management and to have this information in a format that can be easily transmitted between members of the healthcare team. Much effort has been spent to try and find a single test of respiratory function that has sufficient sensitivity and specificity to predict outcome for all pulmonary resection patients. It is now clear that no single test will ever accomplish this. It is useful to assess each patient's respiratory function in three related but largely independent areas such as: respiratory mechanics, pulmonary parenchymal function, and cardio-respiratory interaction. These can be remembered as the basic functional units of extracellular respiration, which are to get atmospheric oxygen: (1) into the alveoli, (2) into the blood, and (3) to the tissues (the process is reversed for carbon dioxide removal).

TABLE 2.1. Post-lobectomy complications and hospital length of stay (LOS).

	All patients	Length of stay <14 days	Length of stay >14 days	Significant for LOS <i>p</i> value
<i>n</i>	4,979	4,628 (93%)	351 (7%)	
Pneumonia	4%	3%	28%	<0.0001
Atelectasis	4%	2%	21%	<0.0001
ARDS	1%	0.5%	11%	<0.0001
Myocardial infarction	0.4%	0.2%	3%	<0.0001
Ileus	1%	0.6%	18%	<0.0001
Renal failure	1.4%	0.9%	9%	<0.0001
Pulmonary embolus	0.3	0.3%	2%	0.02
Atrial arrhythmias	12%	11%	27%	0.07
Air leak >5 days	10%	8%	36%	<0.0001

Based on data from the Society of Thoracic Surgeons Database, 2002–2006, Wright et al. [3]

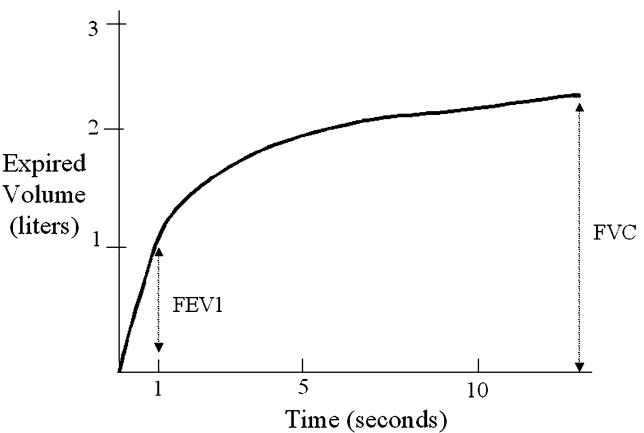


FIG. 2.2. Simple spirometry should be performed in all pulmonary resection patients to assess the forced expiratory volume in 1 s (FEV1) which can then be corrected for the patient's age, sex, and height to give a percentage of the normal predicted value (FEV1%).

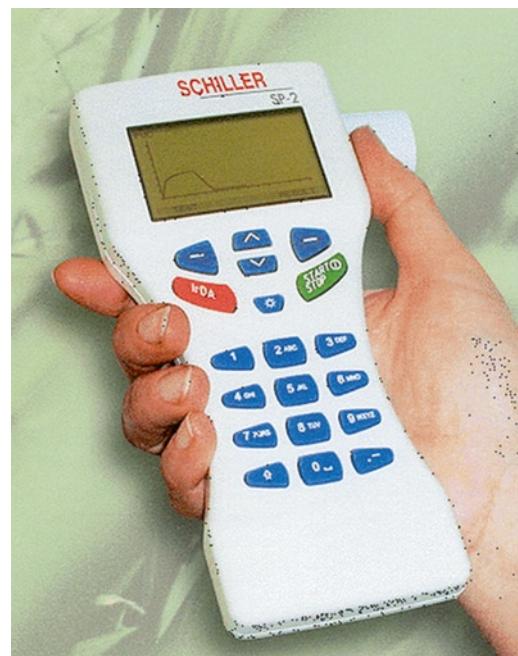


FIG. 2.3. An example of a portable handheld spirometer which can be easily used in the preoperative assessment clinic or at the bedside to measure forced expiratory flow volumes.

Lung Mechanical Function, Spirometry

Many tests of respiratory mechanics and volumes show correlation with post-thoracotomy outcome: FEV1, FVC, maximal voluntary ventilation (MVV), and residual volume/total lung capacity ratio (RV/TLC). For preoperative assessment these values should always be expressed as a percent of predicted volumes corrected for age, sex, and height (e.g., FEV1%). Of these, the most valid single test for post-thoracotomy

respiratory complications is the predicted postoperative FEV1 (ppoFEV1%) [5] which is calculated as:

$$\text{ppoFEV1\%} = \text{preoperative FEV1\%} \times (1 - \text{functional lung tissue removed} / 100)$$

One method of estimating the percent of functional lung tissue is based on a calculation of the number of functioning subsegments of the lung removed (Fig. 2.4). Nakahara et al. [6] found that patients with a ppoFEV1 >40% had no or minor post-resection respiratory complications. Major respiratory complications were only seen in the subgroup with ppoFEV1 <40% (although not all patients in this subgroup developed respiratory complications) and 10/10 patients with ppoFEV1 <30% required postoperative mechanical ventilatory support. These key threshold ppoFEV1 values: 40 and 30% are extremely useful to remember when managing these patients. The schema of Fig. 2.4 may be overly complicated and it can be useful to just simply consider the right upper and middle lobes combined as being approximately equivalent to each of the other three lobes with the right lung 10% larger than the left. These data of Nakahara are from work done in the 1980s and subsequent advances, particularly the use of epidural analgesia has decreased the incidence of complications in the ultrahigh-risk (ppo <30%) group [7]. However, a ppoFEV1 value of <40% remains useful as a reference point for the anesthesiologist to identify the patient at increased risk. The ppoFEV1 is the most significant independent predictor of complications among a variety of historical, physical, and laboratory tests for these patients. The usefulness of the ppoFEV1% has been recently revalidated in a study by

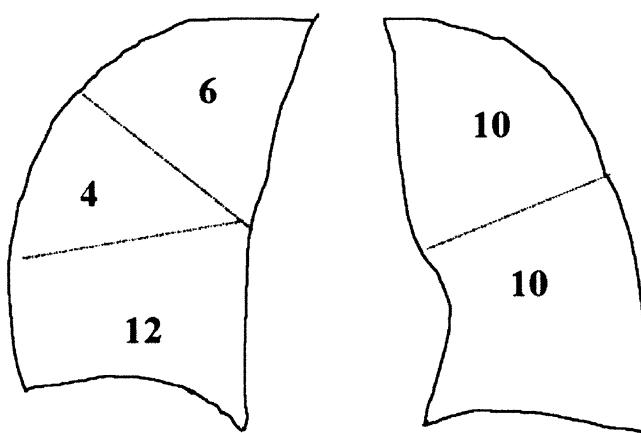


FIG. 2.4. The number of subsegments of each lobe are used to calculate the predicted postoperative (ppo) pulmonary function. There are 6, 4, and 12 subsegments in the right upper, middle, and lower lobes. There are 10 subsegments in both the left upper and lower lobes, for a total of 42 subsegments. Following removal of a functioning right lower lobe, a patient would be expected to lose 12/42 (29%) of their respiratory reserve. If the patient has a preoperative FEV1 (or DLCO) 70% of predicted, the patient would be expected to have a ppoFEV1 = $70\% \times (1 - 29/100) = 50\%$.

Win et al. [8]. However, these authors suggest that with an aging surgical population a threshold value of ppoFEV1 45% is more appropriate.

Patients with ppoFEV1 values <40% can be operated on with acceptable morbidity and mortality in certain circumstances. Linden et al. [9], reported on a series of 100 patients with ppoFEV1 <35% who had lung resections for cancer with only one mortality and with a 36% complication rate. Whenever possible, these patients had VATS procedures and thoracic epidural analgesia (TEA). The authors propose an absolute lower limit of acceptability for resection as a ppoFEV1 <20%. It should be appreciated that this report is from a center with a very high volume of thoracic surgery and surgical outcomes for lung cancer are correlated to the volume of surgery. High-volume hospitals had complication and mortality rates (20 and 3% respectively) that were approximately one-half of low-volume hospitals (44 and 6%) [10].

The actual measured postoperative FEV1 will not be the same as the ppoFEV1 for several reasons. First, it is impossible to predict the actual intraoperative surgical trauma to the chest wall and residual lung segments. Most patients will have FEV1 values immediately postoperatively that are less than the ppoFEV1 and these will improve over a period of 6 months [11]. Second, emphysematous patients will tend to have a lung-volume reduction effect on the residual lobe(s) and may exceed their ppoFEV1 if a hyperinflated lobe is resected. The actual postoperative FEV1 has been shown to be a better predictor of outcome than the ppoFEV1 however, the actual postoperative FEV1 is not available preoperatively.

Absolute predicted postoperative values for FEV1 were used in the past to assess patients. Absolute limits for ppoFEV1 such as 0.8 L were suggested as the lower limits of acceptability for resection. However, absolute values for pulmonary function tests do not take into consideration the wide variation in the size of patients who present for thoracic surgery. An absolute FEV1 result of 1 L for an 80-year-old male 5 ft. (152 cm) height is normal (100% of predicted) but an FEV1 of 1 L for a 6 ft. (183 cm) 50-year-old male is severely abnormal (24% predicted). It is important always to consider patients' spirometry results as a percentage of their predicted normal.

Patients at increased risk of respiratory complications (ppoFEV1 <40%) should have complete pulmonary function testing in a pulmonary function laboratory which will include an assessment of lung volumes and airway resistance (Fig. 2.5). These are more sensitive than a simple examination of the FEV1 to FVC ratio to distinguish between obstructive versus restrictive lung pathologies and will confirm the clinical diagnosis of the underlying lung disease. Also, this permits for optimization of intraoperative management during both two-lung and one-lung ventilation by individualization of settings for mechanical ventilation depending on the lung pathology [12]. There are two basic methods of measurement of lung volumes: insoluble gas dilution and plethysmography (Fig. 2.6). Plethysmography is the common method used in pulmonary function laboratories to measure lung volumes

FIG. 2.5. Complete pulmonary function testing will provide data on lung volumes and capacities to differentiate obstructive from restrictive diseases. *FRC* functional residual capacity; *IC* inspiratory capacity; *RV* residual volume; *SVC* slow vital capacity; *ERV* expiratory reserve volume; *TV* tidal volume; *IRV* inspiratory reserve volume; *TLC* total lung capacity. Measuring closing volume and closing capacity requires insoluble gas washout techniques and is not included in routine pulmonary function testing. However, an appreciation of the variable relationship between closing capacity and FRC and the effects of anesthesia on FRC is essential for the anesthesiologist to understand the changes in gas exchange that occur during anesthesia. (Reprinted from Patterson [101], with permission).

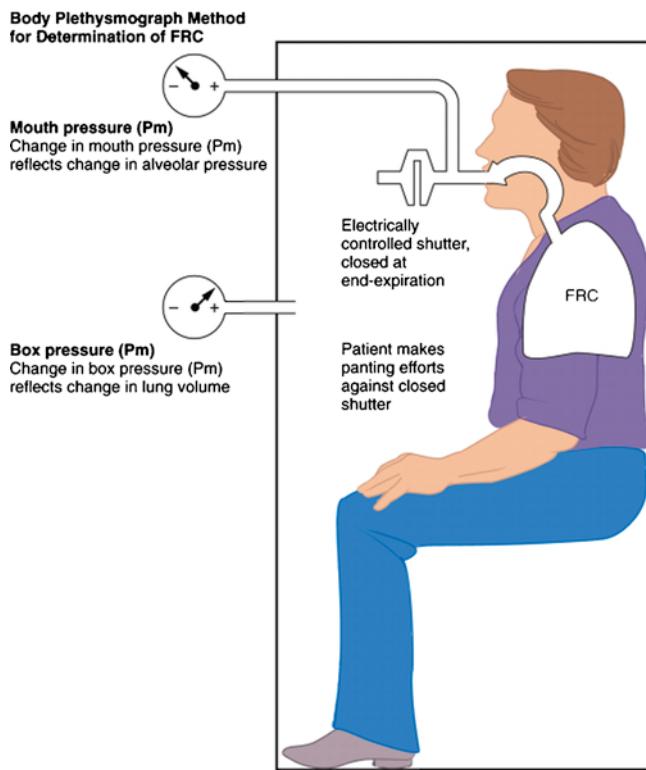
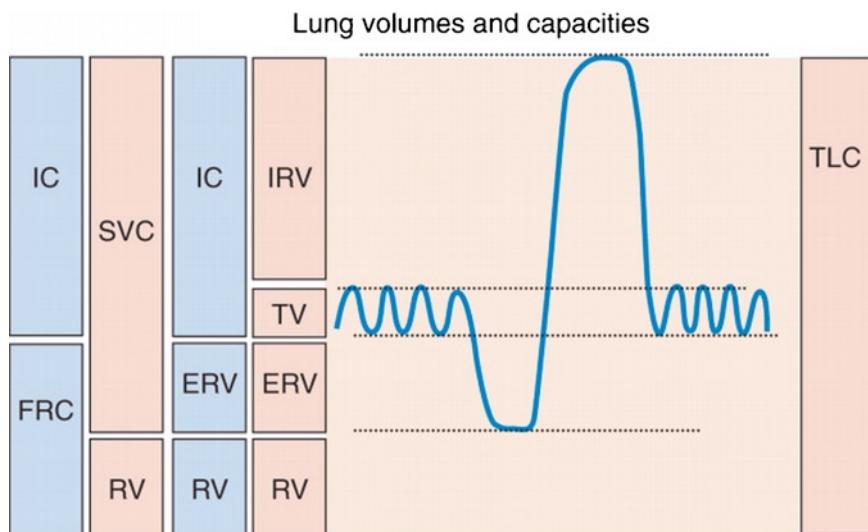


FIG. 2.6. Measurement of lung volumes is commonly performed with whole body plethysmography with the patient seated in an airtight box. Lung volumes can be calculated from changes in the airway and box pressure since the volume of the box is known. (Reprinted from Patterson [101], with permission).

and has largely replaced insoluble gas dilution techniques. The difference (plethysmography-dilution) in measured lung volumes between the two techniques can be used to estimate the volume of bullae in the lung. Previously, maximal breathing capacity was also used to assess patients for pulmonary

resection. This simple test was used in the era of pulmonary resection for tuberculosis and has been replaced by modern spirometry.

Pulmonary Parenchymal Function

As important to the process of respiration as the mechanical delivery of air to the distal airways is the subsequent ability of the lung to exchange oxygen and carbon dioxide between the pulmonary vascular bed and the alveoli. Traditionally, arterial blood gas data such as $\text{PaO}_2 < 60 \text{ mmHg}$ or $\text{PaCO}_2 > 45 \text{ mmHg}$ have been used as cut-off values for pulmonary resection. Cancer resections have now been successfully performed, or even combined with volume reduction, in patients who do not meet these criteria, although they remain useful as warning indicators of increased risk. The most useful test of the gas exchange capacity of the lung is the diffusing capacity for carbon monoxide (DLCO). The DLCO is a reflection of the total functioning surface area of alveolar-capillary interface. This simple noninvasive test which is included with spirometry and plethysmography by most pulmonary function laboratories is a useful predictor of perioperative morbidity and mortality [13]. The corrected DLCO can be used to calculate a post-resection (ppo) value using the same calculation as for the FEV₁ (Fig. 2.7). A ppoDLCO < 40% predicted correlates with both increased respiratory and cardiac complications and is, to a large degree, independent of the FEV₁. The National Emphysema Treatment Trial has shown that patients with a preoperative FEV₁ or DLCO < 20% had an unacceptably high perioperative mortality rate [14]. These can be considered as the absolute minimal values compatible with successful outcome. Complete pulmonary function testing, as performed in a pulmonary function laboratory generates a report with often >15 test results (Fig. 2.8); of these results the two most valid tests for the anesthesiologist to use to assess perioperative risk are the percent predicted FEV₁ and DLCO.

Cardiopulmonary Interaction

The final and perhaps most important assessment of respiratory function is an assessment of the cardiopulmonary interaction. Formal laboratory exercise testing is currently the “gold standard” for assessment of cardiopulmonary function [15] and the maximal oxygen consumption (VO_2 max) is the most useful predictor of post-thoracotomy outcome. The test is performed on a bicycle ergometer or treadmill. Resting measurements are made for 3–5 min. Three minutes of unloaded

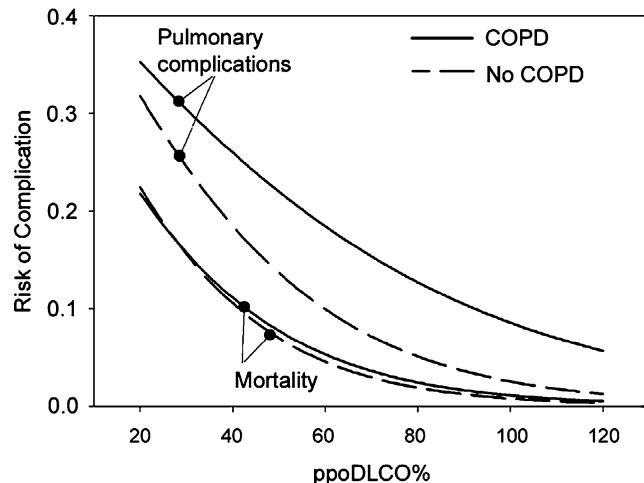


FIG. 2.7. Regression lines for the risk of pulmonary (upper lines) or fatal (lower lines) complications versus predicted postoperative diffusing capacity for carbon monoxide (ppoDLCO%) following lung resection in patients with (solid lines) and without (dashed lines) chronic obstructive pulmonary disease (COPD). Note that both morbidity and mortality increase sharply when the ppoDLCO falls below a threshold value of 40% (Reprinted from Ferguson and Vigneswaran [13], with permission).

cycling is performed as a warm-up period. The workload is incremented at a rate designed to allow reaching maximum work capacity in 8–12 min. The test continues to a point of symptom limitation (e.g., severe dyspnea) or discontinuation by medical staff (e.g., significant ECG abnormalities) or achievement of maximum predicted heart rate. Estimated VO_2 max is based on the patient’s age, sex, and height. For sedentary males it is estimated as VO_2 max (mL/min) = (height (cm) – age (years)) \times 20, i.e., for a 50-year-old male, height 170 cm, weight 70 kg, the predicted VO_2 max = $((170 - 50) \times 20) / 70 = 34$ mL/kg/min. For a sedentary woman, age 50, 160 cm, 60 kg, estimated VO_2 max = $((160 - 50) \times 14) / 60 = 26$ mL/kg/min (for comparison: the highest VO_2 max recorded is 85 mL/kg/min by the American cyclist Lance Armstrong in 2005 [16]).

The risk of morbidity and mortality is unacceptably high if the preoperative VO_2 max is <15 mL/kg/min [17]. Few patients with a VO_2 max >20 mL/kg/min have respiratory complications. Exercise testing is particularly useful to differentiate between patients who have poor exercise tolerance due to respiratory versus cardiac etiologies (Fig. 2.9). More recently, the anaerobic threshold measured during exercise testing has been suggested as a predictor of postoperative complications [18]. The anaerobic threshold is the exercise level at which lactate begins to accumulate in the blood and anaerobic metabolism begins. The anaerobic threshold is approximately 55% of VO_2 max in untrained individuals but rises to $>80\%$ in trained athletes. The anaerobic threshold can be documented by repeated blood lactate analysis during exercise or by a threshold increase in CO_2 production above the initial respiratory quotient (ratio of CO_2 production to O_2 consumption, commonly approximately 0.8). A threshold value for AT of <11 mL/kg/min has been suggested as a marker for increased risk but this has not been well validated [19].

FIG. 2.8. A copy of the Pulmonary Function Laboratory test report for a patient with severe emphysema. Of the 15 different results in this report the two results highlighted, the percent predicted FEV1 and DLCO, are the most useful tests for the anesthesiologist assessing a patient for possible pulmonary resection. This patient had taken a bronchodilator immediately before the test so the usual post-bronchodilator (Post BD) test was not repeated. *Pred. val.* predicted value corrected for the patient’s age, sex, and height. *Obs.* patient’s measured result; VA the single-breath dilutional estimate of TLC from the DLCO.

Test Performed	Pred. val.	Pre BD		Post BD	
		Obs.	%Pred. val.	Obs.	%Pred. val.
Total Lung Capacity (TLC), L	4.2	7.4	175	---	---
Functional Residual Capacity (FRC), L	2.6	6.2	239	---	---
Inspiratory Capacity (IC), L	1.6	1.2	74	---	---
Vital Capacity (VC), L	2.4	1.5	63	---	---
Residual Volume (RV), L	1.8	5.9	322	---	---
RV/TLC Ratio (RV/TLC), %	43	80	184	---	---
Forced Vital Capacity (FVC), L	2.4	1.5	62	---	---
Forced Exp. Volume in 1 sec. (FEV1), L	1.7	0.6	34	---	---
FEV1/FVC Ratio (FEV1/FVC), %	71	39	55	---	---
Max. Exp. Flow @ 50% VC (V50), L/sec	2.4	0.17	7	---	---
Max. Exp. Flow @ 25% VC (V25), L/sec	1.2	0.07	6	---	---
Mid Expiratory Flow 25–75% (FEF 25–75), L/sec	2.0	0.2	12	---	---
Airway Resistance (Raw), cmH ₂ O/L/sec	0.7	2.5	387	---	---
Max. Voluntary Ventilation (MVV), L/min	50	---	---	---	---
Lung Diffusion Capacity (DL _{CO}), mL/min/mmHg	12.6	7.5	59	Normal limits: 75–125%	
VA @ BTPS from DL _{CO}	(VA@BTPS), L	4.2	2.5	60	---

NOTE: %Pred. values are BOLD when outside of normal limits. (All except Raw & DL_{CO} values.)

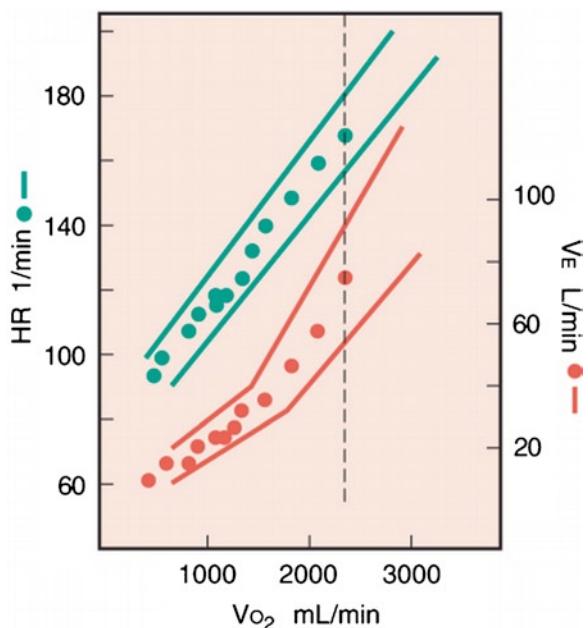


FIG. 2.9. A normal cardiopulmonary exercise test result. As the patient exercises, the increase in oxygen consumption (horizontal axis) is plotted against the heart rate (green dots, left vertical axis) and the minute ventilation (V_E , orange dots, right vertical axis). Normal responses for heart rate and ventilation lie within the green and orange lines. The vertical dashed line is the predicted upper limit of normal based on age. Patients with primarily cardiac causes for exercise limitation will show an excessive increase in heart rate with exercise. Patients with primarily respiratory limitation will show a disproportionate increase in ventilation. Patients with pulmonary vascular disease will have both abnormal heart rate and ventilation responses. (Reprinted from Patterson [101], with permission).

Complete laboratory exercise testing is time-consuming and thus expensive. It is generally not cost-effective to use as a routine part of the preoperative assessment for all pulmonary resection patients. Several alternatives have been demonstrated to be valid surrogate tests for pre-thoracotomy assessment. The distance that a patient can walk during a 6-min test (6MWT) shows an excellent correlation with VO_2 max and requires little or no laboratory equipment (Fig. 2.10). For patients with moderate or severe COPD, the 6MWT distance can be used to estimate the VO_2 max by dividing by a figure of 30 (i.e., 600 m distance is equivalent to a VO_2 max of $600/30=20$ mL/kg/min) [20]. Some centers also assess the fall in oximetry (SpO_2) during exercise. Patients with a decrease of $SpO_2 >4\%$ during exercise (stair climbing 2 or 3 flights or equivalent) [21] are at increased risk of morbidity and mortality. Post-resection exercise capacity can also be estimated based on the amount of functioning lung tissue removed (see Fig. 2.4). An estimated $ppoVO_2$ max <10 mL/kg/min can be considered a contraindication to pulmonary resection. In a small series [22] mortality was 100% (3/3) patients with a $ppoVO_2$ max <10 mL/kg/min.

The traditional, and still useful, test in ambulatory patients is stair climbing [23]. Stair climbing is done at the patient's own pace but without stopping and is usually documented as a certain number of flights. There is no exact definition for a "flight" but 20 steps at 6 in/step is a frequent value. The ability to climb five flights correlates with a VO_2 max >20 mL/kg/min and climbing two flights corresponds to a maximal oxygen consumption (VO_2 max) of 12 mL/kg/min. A patient unable to climb two flights is extremely at high-risk [24].

After pulmonary resection there is a degree of right ventricular dysfunction that seems to be in proportion to the amount

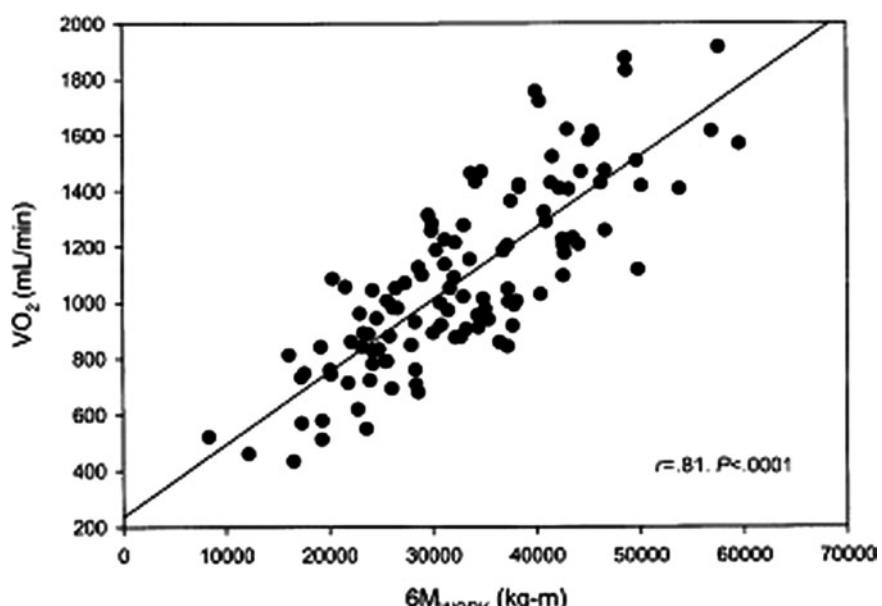


FIG. 2.10. The maximal oxygen consumption VO_2 (mL/min) shows a strong correlation with work ($6M_{work}$) for patients with moderate or severe COPD during a 6 min. walk test. Work = distance traveled \times weight (kg \times m). A 70 kg patient who walks 450 m does 31,500 kg/m of work which correlates with an estimated VO_2 max of 1,100 mL/min (or 16 mL/kg/min). A simple estimate of the VO_2 max can be made by dividing the 6-min walk distance by 30 (i.e., 450 m/30 = 15 mL/kg/min). (Reprinted from Carter et al. [20], with permission.).

of functioning pulmonary vascular bed removed. The exact etiology and duration of this dysfunction remains unknown. Clinical evidence of this hemodynamic problem is minimal when the patient is at rest but is dramatic when the patient exercises leading to elevation of pulmonary vascular pressures, limitation of cardiac output, and absence of the normal decrease in pulmonary vascular resistance usually seen with exertion [25].

Regional Lung Function

Prediction of post-resection pulmonary function can be further refined by assessment of the preoperative contribution of the lung or lobe to be resected by imaging of regional lung function [26]. If the lung region to be resected is nonfunctioning or minimally functioning, the prediction of postoperative function can be modified accordingly [27]. This is particularly useful in pneumonectomy patients and regional lung function imaging should be ordered for any potential pneumonectomy patient who has a preoperative FEV1 and/or DLCO < 80% (i.e., ppo values < 40% predicted). Regional lung function imaging can be performed by three techniques: radionuclide ventilation/perfusion (*V/Q*) lung scanning, pulmonary quantitative

CT-scanning, or three-dimensional dynamic perfusion magnetic resonance imaging (MRI).

Ventilation/perfusion lung scanning is the gold standard. Regional ventilation is assessed by scanning after inhalation of a radiolabeled insoluble gas (commonly xenon-133). Regional lung perfusion is assessed by scanning after intravenous injection of radiolabeled particles that are trapped in the pulmonary capillaries (commonly: technetium-99 m macroaggregated albumin) (Fig. 2.11). Actual postoperative lung function has shown a high correlation with predicted values based on preoperative *V/Q* scanning for FEV1 ($r=0.92$), DLCO ($r=0.90$) and VO_2 max ($r=0.85$). Prediction is more accurate for post-pneumonectomy versus post-lobectomy values. If there is a discrepancy between the ventilation and perfusion scan results, it is preferable to use the result which attributes the larger proportion of ventilation or perfusion to the diseased lung to estimate the post-resection pulmonary function (i.e., worst case scenario).

Quantitative CT lung scans can be used to estimate post-resection values [28]. Each CT slice is quantified for areas of normal parenchyma, emphysema, and atelectasis. The contribution of each lobe or lung can be estimated based on the volume of normal parenchyma and then used to predict postoperative lung function. Quantitative CT primarily focuses on areas of ventilation and is more accurate for post-lobectomy versus post-pneumonectomy values. Predicted postoperative values for FEV1 and DLCO were comparable to those derived from *V/Q* scans but less accurate for VO_2 max. This is a newer technique than *V/Q* scanning and requires specific imaging expertise. However, due to the routine preoperative CT scanning of most pulmonary resection patients it may become more available.

Dynamic MRI uses estimates of regional pulmonary blood volume to assess regional blood flow [29]. This is the newest of the three techniques and is not widely used. It has shown a high level of correlation between predicted and actual values for postoperative FEV1. It has not been assessed for predicting DLCO or VO_2 max.

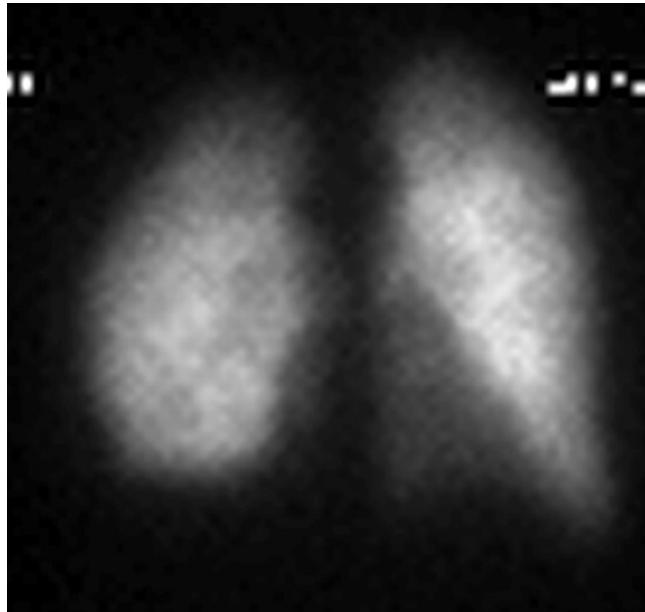


FIG. 2.11. Perfusion scan of a patient with a right lung tumor being assessed for possible pneumonectomy. The perfusion of the right lung was 37% and the left 63%. Preoperative FEV1 = 74% predicted and DLCO = 70%. Based on the anatomic number of subsegments to be excised the predicted postoperative (ppo) FEV1 = $74 \times 22/42 = 39\%$ and the ppoDLCO = $70 \times 22/42 = 37\%$. Using the regional lung imaging to predict postoperative values, the ppoFEV1 = $74 \times 0.63 = 47\%$ and the ppoDLCO = $70 \times 0.63 = 44\%$, which are above the threshold values for increased perioperative risk.

Split-Lung Function and Other Lung Function Tests

A variety of methods have been described to try and simulate the postoperative respiratory situation by preoperative unilateral exclusion of a lung or lobe with an double-lumen tube or bronchial blocker and/or by pulmonary artery balloon occlusion of a lung or lobe artery [30]. These tests have not shown sufficient predictive validity for universal adoption in lung resection patients. Lewis et al. [31] have shown that in a group of patients with COPD (ppoFEV1 < 40%) undergoing pneumonectomy, there were no significant changes in the pulmonary vascular pressures intraoperatively when the pulmonary artery was clamped but the right ventricular ejection fraction (RVEF) and cardiac output decreased. Echocardiography

may offer more useful information than vascular pressure monitoring in these patients [32]. Split-lung function studies have been replaced in most centers by a combined assessment involving, spirometry, DLCO, exercise tolerance, and imaging of regional lung function.

Combination of Tests

No single test of respiratory function has shown adequate validity as a sole preoperative assessment. Prior to surgery, an estimate of respiratory function in all three areas: lung mechanics,

parenchymal function, and cardiopulmonary interaction should be made for each patient. These three aspects of pulmonary function form the “three-legged stool” which is the foundation for pre-thoracotomy respiratory assessment (Fig. 2.12). These data can then be used to plan intra- and postoperative management (Fig. 2.13) and also to alter these plans when intraoperative surgical factors necessitate that a resection becomes more extensive than foreseen. If a patient has a $\text{ppoFEV}_1 > 40\%$, it should be possible for that patient to be extubated in the operating room at the conclusion of surgery assuming the patient is alert, warm, and comfortable (“AWaC”). Patients with a $\text{ppoFEV}_1 < 40\%$ will usually comprise about one fourth of an average thoracic surgical population. If the ppoFEV_1 is $> 30\%$ and exercise tolerance and lung parenchymal function exceed the increased risk thresholds then extubation in the operating room should be possible depending on the status of associated medical conditions. Those patients in this subgroup who do not meet the minimal criteria for cardiopulmonary and parenchymal function should be considered for staged weaning from mechanical ventilation postoperatively so that the effect of the increased oxygen consumption of spontaneous ventilation can be assessed. Patients with a ppoFEV_1 20–30% and favorable predicted cardio-respiratory and parenchymal function can be considered for early extubation if thoracic epidural analgesia (TEA) is used, or if the resection is performed with VATS. Otherwise, these patients should have a postoperative staged weaning from mechanical ventilation. In the borderline group (ppoFEV_1 30–40%) the presence of several associated factors and diseases which should be documented during the preoperative assessment will enter into the considerations for postoperative management (see below).

Jordan and Evans have outlined a protocol for planned elective admission of pulmonary resection patients to the intensive care unit postoperatively [33]. In their scheme, patients age > 70 years or with fibrotic lung disease or with positive cardiovascular risk assessment or with an elevated ASA score or poor lung function (preoperative $\text{FEV}_1 < 47\%$) would be admitted to ICU. Others would go to the recovery unit then a monitored ward bed.

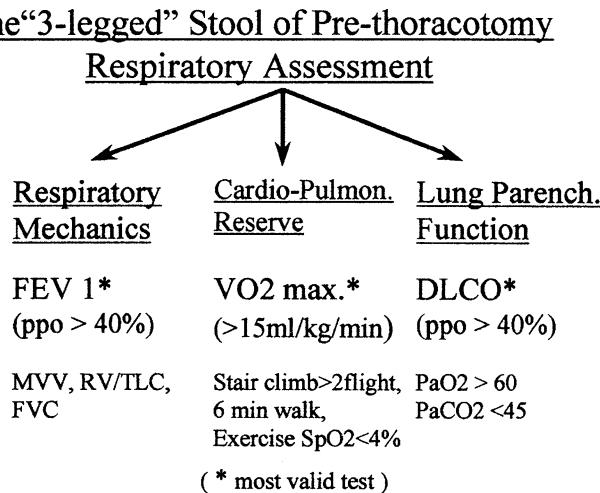


FIG. 2.12. The “three-legged stool” of pre-thoracotomy respiratory assessment involves evaluation of lung mechanical function, pulmonary parenchymal function, and cardiopulmonary interaction for each patient. The most valid test in each area is denoted by asterisk. The threshold values below which risk increases are in parentheses. *ppo* predicted postoperative value as a percent of the patient’s predicted normal value; *FEV* 1 forced expiratory volume in 1 s; *MVV* maximal voluntary ventilation; *RV/TLC* residual volume/total lung capacity ratio; *FVC* forced vital capacity; *VO₂ max.* maximal oxygen consumption; *SpO₂* pulse oximetry; *DLCO* lung diffusing capacity for carbon monoxide. *PaO₂* and *PaCO₂* values in mmHg.

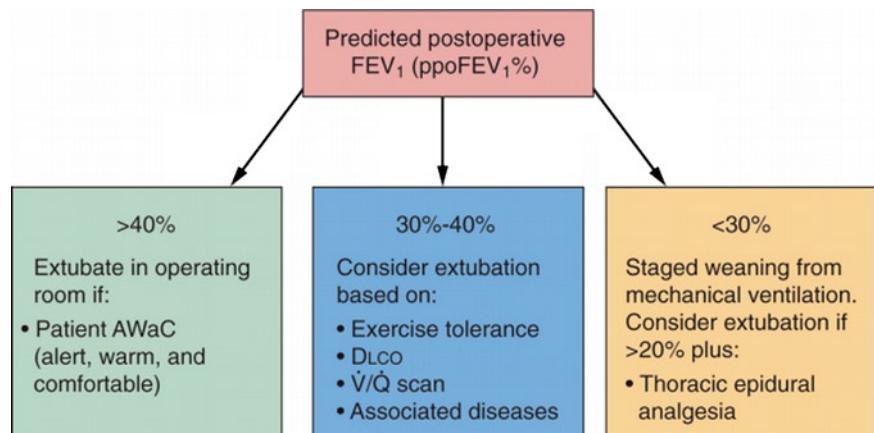


FIG. 2.13. Anesthetic management guided by preoperative assessment and the amount of functioning lung tissue removed during surgery. \dot{V}/\dot{Q} scan=ventilation/perfusion lung scan or other regional lung imaging.

Concomitant Medical Conditions

Cardiac Disease

Cardiac complications are the second most common cause of perioperative morbidity and mortality in the thoracic surgical population. The commonest major cardiac complications are myocardial ischemia/infarction and arrhythmias.

Ischemia

Since the majority of pulmonary resection patients have a smoking history, they already have one risk factor for coronary artery disease (other factors include male sex, heredity, diabetes, obesity, high blood pressure and elevated cholesterol). Elective pulmonary resection surgery is regarded as an “intermediate risk” procedure in terms of perioperative cardiac ischemia [34]. The overall documented incidence of post-thoracotomy ischemia is 5% and peaks on day 2–3 postoperatively (Fig. 2.14) [35]. Beyond the standard history, physical and electrocardiogram, further routine testing for cardiac disease does not appear to be cost-effective for all pre-thoracotomy patients.

For patients with a history suggesting coronary artery disease the preoperative pathways for cardiac investigation prior to pulmonary resection are becoming increasingly complex (Fig. 2.15). The American College of Cardiology and American Heart association have developed algorithms for cardiac investigations in these patients. Patients with intermediate clinical predictors of increased cardiac risk (stable angina, diabetes, etc.) who have adequate functional capacity do not need further cardiac investigation prior to pulmonary surgery. Patients with these intermediate predictors and poor functional capacity should have noninvasive testing of myocardial perfusion at rest and during stress. The estimate of myocardial perfusion can be performed by nuclear medicine (technetium sestamibi or thallium injection) or transthoracic echocardiography at rest and during stress. The stress can be either with exercise or by injection of a coronary vasodilator (dipyridamole) or an inotrope (dobutamine). Based on the results from

studies in vascular surgery [36], it can be extrapolated that patients with normal perfusion or who have areas of reversibility in <20% of myocardial segments can proceed to surgery without further cardiac investigation. For patients who have a result on myocardial perfusion testing that is inconclusive, CT coronary angiography is a noninvasive option (Fig. 2.16) [37]. CT angiography has a high sensitivity for coronary stenosis but is less specific. Thus, a patient with a normal CT coronary angiogram can proceed to surgery. However, an abnormal CT coronary angiogram will then require further investigation which will probably necessitate cardiac catheterization.

For patients who have major reversibility on a myocardial perfusion test, the diagnostic and therapeutic pathway is less clear. The standard recommendation is to proceed to cardiac catheterization. However, in individual circumstances it could be an option to proceed with a minor diagnostic procedure (such as an endobronchial ultrasound or mediastinoscopy) first if there is a reasonable possibility that the patient may not have a resectable cancer. Or, it may be considered to proceed with the pulmonary resection with very tight perioperative hemodynamic control since it is not clear that coronary intervention improves perioperative outcome in patients who are not clear candidates for intervention outside the perioperative period [38]. The wisdom of elective perioperative β -blockade in these patients is debatable [39]. β -blockade may decrease the perioperative cardiac risk but increase the risk of stroke. Patients who have an indication for β -blockade apart from the perioperative context should be started and continued on these medications perioperatively, appreciating that many thoracic surgical patients have reactive airways disease that may be exacerbated by β -blockade. The use of β -blockers otherwise should be guided by specific hemodynamic indications.

For patients who require coronary catheterization, the results may necessitate angioplasty with or without stenting or coronary artery bypass surgery before or at the same time as pulmonary surgery (see Chap. 32). It is very important that the interventional cardiologist be made aware of the patient’s diagnosis and the perioperative context prior to angiography. If bare metal coronary stents are placed, the patient will require dual antiplatelet therapy with a thienopyridine and aspirin for

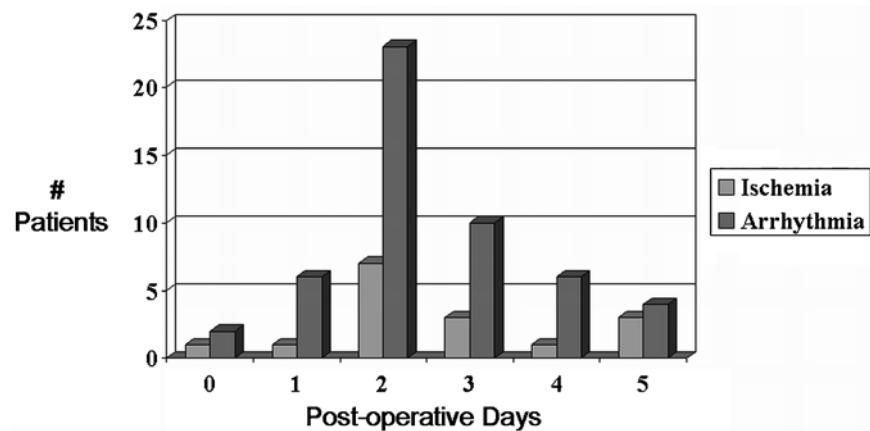


FIG. 2.14. Number (hash) of patients (total $n >300$) who developed myocardial ischemia or arrhythmias postoperatively following pulmonary resections for lung cancer. Both the incidence of arrhythmia (primarily atrial fibrillation) and ischemia peak on postoperative day 2. (Based on data from von Knorring et al. [35]).

FIG. 2.15. An algorithm for cardiac risk assessment prior to noncardiac thoracic surgery based on Fleisher et al. [34] (see text). *OR* operating room (i.e., proceed with surgery without further cardiac investigation). *Cath.* coronary catheterization. Once a patient is found to have an abnormal result on noninvasive testing of myocardial perfusion, choosing the optimal pathway becomes complicated and requires a combined consultation with the surgeon, cardiologist, and patient.

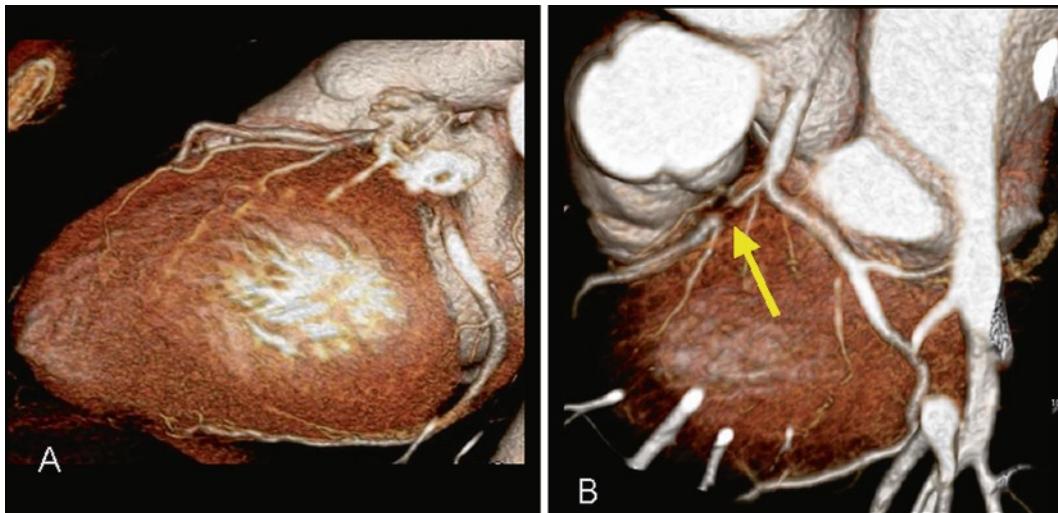
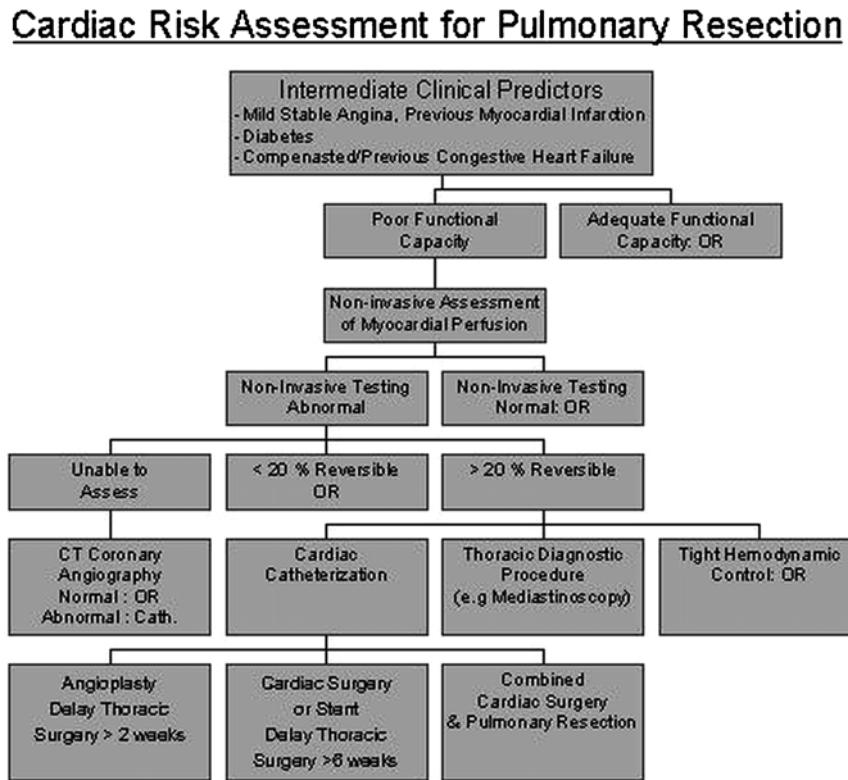


FIG. 2.16. *CT* Coronary angiograms of two different patients. (a) A lateral view of the left ventricle showing a normal left anterior descending (seen superior to the left ventricle in this view) and circumflex (seen to the right of and then below the left ventricle) coronary arteries. Patients with normal coronary arteries on *CT* angiography do not need further investigation for myocardial ischemia. (b) A view of the left ventricle from above in a patient with a lesion in the left anterior descending artery (arrow) just distal to the bifurcation of the left main coronary artery. This patient will require invasive coronary catheterization to determine the precise severity of the lesion and possibly for percutaneous intervention such as stenting. (Images courtesy of Dr. Elsie Nguyen, Department of Medical Imaging, Toronto General Hospital).

4–6 weeks before the thienopyridine can be stopped (and the aspirin continued) preoperatively. In some cases, this is an acceptable delay before a major pulmonary resection or other thoracic surgery. However, if drug-eluting stents are placed the risk of stent stenosis, which is often fatal, is

unacceptable if dual antiplatelet therapy is discontinued in the first 12 months [40]. This is generally not an acceptable delay for cancer surgery.

Timing of lung resection surgery following a myocardial infarction is always a difficult decision. Limiting the delay

to 4–6 weeks in a medically stable and fully investigated and optimized patient seems acceptable after myocardial infarction. The anesthesiologist needs to appreciate that the preoperative assessment and the therapeutic options for patients with significant coronary artery disease presenting for lung surgery is becoming very complicated and no single algorithm can be applied given the complexities of each individual case and the local availability of diagnostic equipment and personnel. Each of these patients needs to be managed by a team consultation that includes the thoracic surgeon, the cardiologist, the anesthesiologist, and the patient and family. The management of a patient who is discovered to have an incidental lung lesion during preoperative assessment for coronary artery or cardiac valvular surgery is discussed in Chap. 32.

Arrhythmias

The management of post-thoracotomy arrhythmias is discussed in Chap. 44. Arrhythmias are a common complication of pulmonary resection surgery and the incidence is 30–50% of patients in the first week postoperatively when Holter monitoring is used [41]. Of these arrhythmias, 60–70% are atrial fibrillation. Several factors correlate with an increased incidence of arrhythmias, these include: extent of lung resection (pneumonectomy 60% vs. lobectomy 40% vs. non-resection thoracotomy 30%), intra-pericardial dissection, intraoperative blood loss, and age of the patient. Extrapleural pneumonectomy patients are a particularly high-risk group [42].

Two factors in the early post-thoracotomy period interact to produce atrial arrhythmias.

1. Increased flow resistance through the pulmonary vascular bed due to permanent (lung resection) or transient (atelectasis, hypoxemia) causes, with attendant strain on the right side of the heart.
2. Increased sympathetic stimuli and oxygen requirements, maximal on the second postoperative day as patients begin to mobilize.

In pneumonectomy patients vs. lobectomy patients, followed for 24 h. with RVEF catheters, there was a significant fall of RVEF on the first postoperative day. This was accompanied by an increase in right ventricular size and in pulmonary artery pressures. Pneumonectomy patients did not demonstrate the early postoperative increase in oxygen delivery, oxygen consumption, or cardiac index as seen in lobectomy patients [43]. This suggests that in some pneumonectomy patients the right heart may not be able to increase its output adequately to meet the usual postoperative stress. Transthoracic echocardiographic studies have shown that pneumonectomy patients develop an increase in right ventricular systolic pressure as measured by the tricuspid regurgitation jet (TRJ) on postoperative day 2 but not on day 1. An increase in TRJ velocity has been associated with post-thoracotomy supraventricular tachyarrhythmias [32]. Patients with COPD are more resistant to pharmacologic rate control when they develop post-thoracotomy atrial fibrillation and often require multiple drugs [44].

A wide variety of antiarrhythmics have been tried to decrease the incidence of atrial arrhythmias after lung surgery. The best known of these are digoxin preparations. It has been demonstrated that digoxin does not prevent arrhythmias after pneumonectomy or other intrathoracic procedures. Other agents which have been tried to prevent post-thoracotomy arrhythmias include: β -blockers, verapamil, and amiodarone. All of these agents decrease arrhythmias in thoracic patients. However, they are all associated with side effects that preclude their widespread application in this surgical population. At present, diltiazem is the most useful drug for post-thoracotomy arrhythmia prophylaxis [45]. It seems that atrial arrhythmias are only a symptom of the dysfunctional right heart and preventing the symptom does not solve the underlying problem. In one study [46] patients who subsequently developed atrial tachyarrhythmias could be identified in the early postoperative period by their right ventricular response to the withdrawal of supplemental oxygen. On the first postoperative day, a decrease of FiO_2 from 0.35 to 0.21 caused a significant rise of right ventricular end-diastolic pressure (RVEDP) in the patients who subsequently developed arrhythmias. TEA with local anesthetics has been suggested to decrease the incidence of arrhythmias. This effect is theorized to be due to increasing the myocardial refractory period, decreasing ventricular diastolic pressures, and improving endocardial/epicardial blood flow ratios [47]. However, the evidence for this is limited.

Age

Perioperative management of the geriatric patient for thoracic surgery is discussed in Chap. 25. There is no maximum age that is a cut-off for pulmonary resection surgery. In one series, the operative mortality in a group of patients 80–92 years of age was 3%, a very respectable figure [48]. However, the rate of respiratory complications (40%) was double that expected in a younger population, and the rate of cardiac complications (40%), particularly arrhythmias, was nearly triple that which would be seen in younger patients. In the elderly, thoracotomy should be considered a high-risk procedure for cardiac complications and cardiopulmonary function is the most important part of the preoperative assessment. An algorithm for the cardiac assessment of the geriatric patient for thoracic surgery is presented in Fig. 2.17. Exercise tolerance seems to be the primary determinant of outcome in the elderly [49]. The ACC/AHA guidelines [34] suggest that with adequate functional capacity, patients with “intermediate” predictors of coronary artery disease do not need further cardiac assessment. However, this recommendation should not be extrapolated to elderly patients. The ACC/AHA guidelines define “adequate functional capacity” as four metabolic equivalents (METS). One MET is the basal resting energy output which is commonly equated to an oxygen consumption of 3.5 mL/kg/min. Four METS is the equivalent of climbing one flight of stairs (Table 2.2) which does not represent an adequate level of exercise capacity for a geriatric patient for major pulmonary resection. The elderly should have, as a minimum cardiac

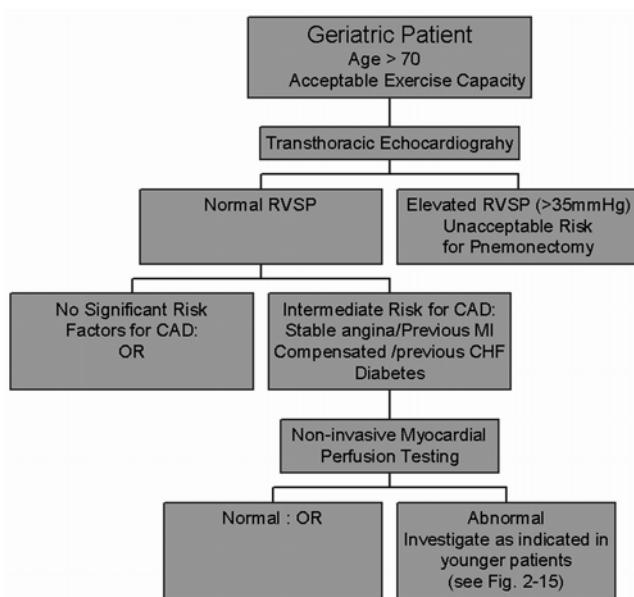


FIG. 2.17. An algorithm for preoperative cardiac investigation in a geriatric patient prior to pulmonary resection surgery. *RVSP* right ventricular systolic pressure estimated by echocardiography; *CAD* coronary artery disease; *OR* operating room (i.e., proceed with surgery without further cardiac investigation).

TABLE 2.2. Energy consumption in metabolic equivalents (METS) of various activities.

Activity	METS
Sitting quietly	1
Walking 1 block	2
Playing the accordion	2
Climbing 1 flight stairs	4
Sexual intercourse ^a	6
Bowling ^a	8
Ice Hockey	8
Running 6 mph	10
Cross country ski racing	14

MET=basal oxygen consumption=3.5 mL/kg/min

Based on data from Hlatky et al. [102]; Fleisher et al. [34]; Ainsworth et al. [103]

^aBowling and sexual intercourse are given fewer METS in some classifications

investigation, a transthoracic echocardiogram, to rule out pulmonary hypertension. Although, the mortality resulting from lobectomy among the elderly is acceptable, the mortality from pneumonectomy, particularly right pneumonectomy, is excessive [50]. Geriatric patients with intermediate risk indicators of coronary artery disease should also have noninvasive myocardial perfusion testing.

Renal Dysfunction

Renal dysfunction following pulmonary resection surgery is associated with a high mortality. College and Goldstraw [51]

TABLE 2.3. Factors associated with an increased risk of post-thoracotomy renal impairment.

Previous history of renal impairment
Diuretic therapy
Pneumonectomy
Postoperative infection
Blood loss requiring transfusion
Preoperative cisplatin chemotherapy

reported a perioperative mortality of 19% (6/31) in patients who developed a significant elevation of serum creatinine in the post-thoracotomy period, compared to 0% (0/99) in those who did not show any renal dysfunction. The factors which were associated with an elevated risk of renal impairment are listed in Table 2.3. Nonsteroidal anti-inflammatory agents (NSAIDS) were not associated with renal impairment in this series but are clearly a concern in any thoracotomy patient with an increased risk of renal dysfunction. The high mortality in pneumonectomy patients from either renal failure or postoperative pulmonary edema emphasizes the importance of fluid management in these patients [52] and the need for close and intensive perioperative monitoring, particularly in those patients on diuretics or with a history of renal dysfunction. Increased preoperative creatinine is associated with an increased incidence of prolonged postoperative endotracheal intubation after lung resection [53]. The importance of renal dysfunction, either preoperative dialysis or a serum creatinine value >2 mg/dL (>175 µmol/L), as a predictor for prolonged length of stay after lobectomy was reconfirmed in an analysis of the Society of Thoracic Surgery database for the period 2002–2006 [3].

Chronic Obstructive Pulmonary Disease

The most common concurrent illness in the thoracic surgical population is chronic obstructive pulmonary disease (COPD) which incorporates three disorders: emphysema, peripheral airways disease, and chronic bronchitis. Any individual patient may have one or all of these conditions, but the dominant clinical feature is impairment of expiratory airflow [54]. Assessment of the severity of COPD has traditionally been on the basis of the FEV1% of predicted values. The American Thoracic Society categorizes Stage I >50% predicted FEV1% (this category previously included both “mild” and “moderate” COPD), Stage II: 35–50%, and Stage III <35%. Life expectancy may be less than 3 years in Stage III patients >60 years of age. Stage I patients should not have significant dyspnea, hypoxemia, or hypercarbia and other causes should be considered if these are present. A complete discussion of perioperative management of patients with COPD is presented in Chap. 24. Of specific importance in the preoperative assessment of the patient with COPD prior to pulmonary resection is to assess for chronic carbon dioxide retention and to initiate therapy for any potentially treatable complications of COPD.

Carbon Dioxide Retention

Many stage II or III COPD patients have an elevated PaCO_2 at rest. It is not possible to differentiate these “ CO_2 -retainers” from non-retainers on the basis of history, physical examination, or spirometric pulmonary function testing [1]. This CO_2 -retention seems to be more related to an inability to maintain the increased work of respiration (W_{resp}) required to keep the PaCO_2 normal in patients with mechanically inefficient pulmonary function and not primarily due to an alteration of respiratory control mechanisms [55]. The PaCO_2 rises in these patients when a high FiO_2 is administered due to a relative decrease in alveolar ventilation [56] and an increase in alveolar dead space and shunt by the redistribution of perfusion away from lung areas of relatively normal V/Q matching to areas of very low V/Q ratio because regional hypoxic pulmonary vasoconstriction (HPV) is decreased [57] and also due to the Haldane effect [58]. However, supplemental oxygen must be administered to these patients postoperatively to prevent the hypoxemia associated with the unavoidable fall in functional residual capacity (FRC). The attendant rise in PaCO_2 should be anticipated and monitored. To identify these patients preoperatively, all stage II or III COPD patients need an arterial blood gas. Also, it is important to know the patient’s baseline preoperative PaCO_2 to guide weaning if mechanical ventilation becomes necessary in the postoperative period.

Preoperative Therapy of COPD

There are four treatable complications of COPD that must be actively sought and therapy begun at the time of the initial pre-thoracotomy assessment. These are: atelectasis, bronchospasm, respiratory tract infections, and pulmonary edema (see Table 2.4). Atelectasis impairs local lung lymphocyte and macrophage function predisposing to infection [59]. Pulmonary edema can be very difficult to diagnose by auscultation in the presence of COPD and may present very abnormal radiological distributions (unilateral, upper lobes, etc.) [60]. Bronchial hyperreactivity may be a symptom of congestive failure [61] or may represent an exacerbation of reversible airways obstruction. All COPD patients should receive maximal bronchodilator therapy as guided by their symptoms. Only 20–25% of COPD patients will respond to corticosteroids. In a patient who is poorly controlled on sympathomimetic and anticholinergic bronchodilators, a trial of corticosteroids may be beneficial [62]. It is not clear if corticosteroids are as

TABLE 2.4. Concurrent problems that should be treated prior to anesthesia in COPD patients.

Problem	Method of diagnosis
Bronchospasm	Auscultation
Atelectasis	Chest X-ray
Infection	History, sputum analysis
Pulmonary edema	Auscultation, chest X-ray

beneficial in COPD as they are in asthma, pharmacotherapy for reactive airway diseases is discussed in Chap. 8.

Physiotherapy

Patients with COPD have fewer postoperative pulmonary complications when a perioperative program of intensive chest physiotherapy is initiated preoperatively [63]. Among COPD patients, those with excessive sputum benefit the most from chest physiotherapy. Among the different modalities available (cough and deep breathing, incentive spirometry, PEEP, CPAP, etc.) there is no clearly proven superior method. The important variable is the quantity of time spent with the patient and devoted to chest physiotherapy. Family members or non-physiotherapy hospital staff can easily be trained to perform effective preoperative chest physiotherapy and this should be arranged at the time of the initial preoperative assessment. Even in the most severe COPD patient, it is possible to improve exercise tolerance with a physiotherapy program. Little improvement is seen before one month. In one small study, eight patients who had been refused pulmonary resection on the basis of poor pulmonary function were enrolled in a 4-week program of pulmonary rehabilitation. After the program, the mean 6-min walk test distance for the group increased 29% and the mean FEV1 increased 5%. All eight patients then had lobectomies without any perioperative mortality [64].

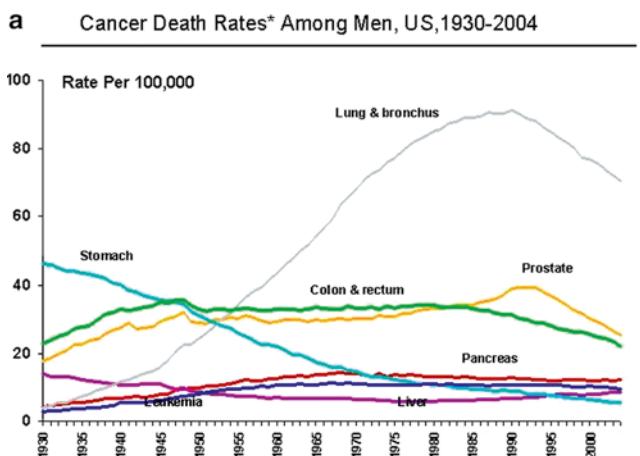
Comprehensive 8–12 week programs of pulmonary rehabilitation involving physiotherapy, exercise, nutrition, and education have been clearly shown to improve functional capacity for patients with severe COPD [65]. These longer programs are generally not an option in resections for malignancy although for nonmalignant resections in severe COPD patients, rehabilitation should be considered. The National Cancer Institute is currently funding a randomized trial to investigate the benefits of a short-term (4 week) program of preoperative pulmonary rehabilitation [66].

Smoking

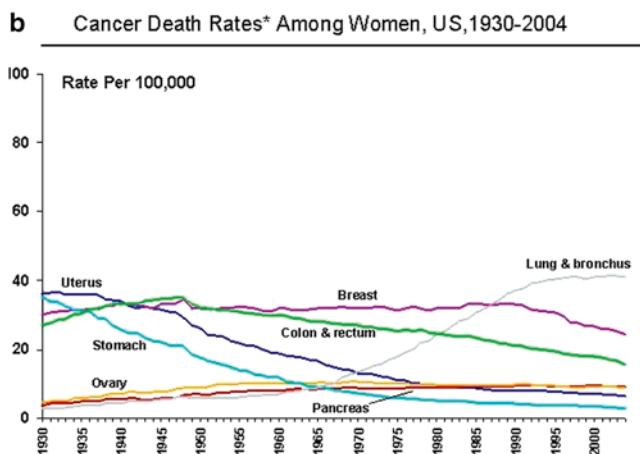
Pulmonary complications are decreased in thoracic surgical patients who cease smoking for >4 weeks before surgery [67]. Carboxyhemoglobin concentrations decrease if smoking is stopped >12 h [68]. It is extremely important for patients to avoid smoking postoperatively. Smoking leads to a prolonged period of tissue hypoxemia. Wound tissue oxygen tension correlates with wound healing and resistance to infection. Wound healing is improved in patients who stop smoking >4 weeks preoperatively [69]. There is no rebound increase in pulmonary complications if patients stop for shorter (<8 week) periods before surgery [70]. The balance of evidence suggests that thoracic surgical patients should be counseled to stop smoking and advised that the longer the period of cessation, the greater the risk-reduction for postoperative pulmonary complications [71].

Perioperative Considerations in Thoracic Malignancies

The majority of patients presenting for major pulmonary surgery will have some type of malignancy. Because the different types of thoracic malignancies have varying implications for both surgery and anesthesia, it is important for the anesthesiologist to have some knowledge of the presentation and biology of these cancers. By far, the most common tumor is lung cancer. It is estimated that at present rates over 210,000 new cases of lung cancer occur in the United States annually. Of these only 26% will be resectable. However, this represents >55,000 patients/year who can be offered potentially curative surgery [72]. Lung cancer is currently the leading cause of cancer deaths in both sexes in North America subsequent to the peak incidence of smoking in the period 1940–1970



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960–2004, US Mortality Volumes 1930–1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960–2004, US Mortality Volumes 1930–1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.

FIG. 2.18. Age adjusted mortality rates for men (a) and women (b) in the United States 1930–2004. Respiratory malignancies have become the leading cause of cancer deaths in both sexes. (Based on data from Vital statistics of the United States: 2008. www.cancer.org).

(Fig. 2.18) [73]. The mortality rate from lung cancer has shown a slight decrease in the last decade for men but has continued to rise in women.

Lung cancer is broadly divided into: small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), with about 75–80% of these tumors being NSCLC. Other less common and less aggressive tumors of the lung include the carcinoid tumors (typical and atypical) and adenoid cystic carcinoma. In comparison to lung cancer, primary pleural tumors are rare. They include the solitary fibrous tumors of pleura (previously referred to as benign mesotheliomas) and malignant pleural mesothelioma (MPM). Asbestos exposure is implicated as a causative effect in up to 80% of MPM. A dose-response relationship is not always apparent and even brief exposures can lead to the disease. An exposure history is often difficult to obtain because the latent period before clinical manifestation of the tumor may be as long as 40–50 years.

Tobacco smoke (both primary and second-hand) is responsible for approximately 90% of all lung cancers and the Epidemiology of lung cancer follows the Epidemiology of cigarette smoking with approximately a three-decade lag time [74]. Other environmental causes include asbestos and radon gas (a decay product of naturally occurring uranium) which act as co-carcinogens with tobacco smoke. For a pack-a-day cigarette smoker, the lifetime risk of lung cancer is approximately 1 in 14. Smoking cessation reduces the risk of lung cancer but never to that for never smokers. Assuming that current mortality patterns continue, cancer will pass heart disease as the leading cause of death in North America in this decade.

Non-Small Cell Cancers

This pathologically heterogeneous group of tumors includes squamous cell, adenocarcinoma, and large-cell carcinoma with several subtypes and combined tumors (Table 2.5). This represents the largest grouping of lung cancers and the vast majority of those that present for surgery. They are grouped together because the surgical therapy, and by inference the anesthetic implications, is similar and depends on the stage of the cancer at diagnosis (Tables 2.6 and 2.7). Survival can approach 80% for stage I lesions. Unfortunately, these represent only a small minority of the potentially resectable lesions. Overall 5-year survival with surgery for NSCLC approaches

TABLE 2.5. Frequency of cell types of primary lung cancers.

Histologic type	Proportion
Adenocarcinoma	40%
Squamous cell	27%
Small cell	19%
Large cell	8%
Bronchoalveolar cell	4%
Mixed adeno/squamous	2%
Carcinoid	1%

Adapted from Barrera et al. [70]

TABLE 2.6. Proposed revised non-small cell lung cancer staging^a.

Stage IA	T1a,b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T1a,b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1,T2	N2	M0
	T3	N1,N2	M0
	T4	N0,N1	M0
Stage IIIB	T4	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1a,b
T1a: ≤2 cm; T1b: >2–≤3 cm			
T2a: >3 cm, ≤5 cm; T2b: >5–7 cm			
T3: >7 cm			
T3: invasion of chest wall, diaphragm, mediastinal pleura, phrenic nerve, parietal pericardium, tumor in the main bronchus <2 cm from the carina			
T3: separate tumor nodule in the same lobe (satellite)			
T4: invades mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina,			
T4: separate tumor nodule in different ipsilateral lobe			
N0			
N1: metastasis in ipsilateral peribronchial, hilar or intrapulmonary nodes			
N2: metastasis in ipsilateral mediastinal nodes, or subcarinal nodes			
N3: metastasis in contralateral mediastinal nodes or ipsilateral or contralateral supraclavicular/scalene nodes			
M1a: malignant pleural effusion, malignant pericardial effusion, separate tumor nodule in contralateral lung			
M1b: distant metastases			
^a Modified from Goldstraw et al. [104]			

TABLE 2.7. Indications for surgery in non-small cell lung cancer.

Stage I A and B	Primary resection, no postoperative chemo/radiotherapy
Stage II	Primary resection, adjuvant postoperative chemotherapy
Stage IIIA, N2 (for patients with N2 disease identified at thoracotomy: postoperative chemotherapy, possibly radiation)	Definitive chemo/radiotherapy, in select patients induction chemo/radiotherapy followed by resection in patients with stable or responding disease
Stage IIIB	Surgery rarely indicated. Chemo/radiotherapy Resection of select T4, N0–1, M0 tumors
Stage IV	Palliative therapy. Possible exception: selected patients with a resected isolated cerebral metastasis

40%. This seemingly low figure must be viewed in the light of an estimated 5-year survival without surgery of <10%.

Although it is not always possible to be certain of the pathology of a given lung tumor preoperatively, many patients will have a known tissue diagnosis at the time of preanesthetic assessment on the basis of prior cytology, bronchoscopy, mediastinoscopy, or transthoracic needle aspiration. This is useful information for the anesthesiologist to obtain preoperatively. Specific anesthetic implications of the different types of lung cancer are listed in Table 2.8.

TABLE 2.8. Anesthetic considerations for different types of lung cancer.

Type	Considerations
Squamous cell	Central lesions (predominantly) Mass effects: obstruction, cavitation Hypercalcemia Hypertrophic pulmonary osteoarthropathy.
Adenocarcinoma	Peripheral lesions Metastases (distant) Growth hormone, corticotropin
Small cell	Central lesions (predominantly) Few surgically treatable Paraneoplastic syndromes Lambert–Eaton syndrome Fast growth rate Early metastases
Carcinoid	Proximal, intra-bronchial
Benign (predominantly)	No association with smoking 5-year survival >90%
Mesothelioma	Carcinoid syndrome (rarely) Intraoperative hemorrhage Direct extension to diaphragm, pericardium, etc.

Adenocarcinoma

Adenocarcinoma is currently the most common NSCLC in both sexes. These tumors tend to be peripheral and often metastasize early in their course, particularly to brain, bone, liver, and adrenal. They often invade extra-pulmonary structures, including chest wall, diaphragm, and pericardium. The majority of Pancoast tumors (see Chap. 29) are now due to adenocarcinomas. A variety of paraneoplastic metabolic factors can be secreted by adenocarcinomas such as growth hormone and corticotropin. Hypertrophic pulmonary osteoarthropathy is particularly associated with adenocarcinoma.

Squamous Cell Carcinoma

This is the subgroup of NSCLC most strongly linked to cigarette smoking. The tumors tend to grow to a large size and metastasize later than others. They tend to cause symptoms related to local effects of a large tumor mass with a dominant endobronchial component, such as: cavitation, hemoptysis, obstructive pneumonia, superior vena cava syndrome, and involvement of mainstem bronchus, trachea, carina, and main pulmonary arteries. Hypercalcemia is specifically associated with this cell type due to elaboration of a parathyroid-like factor and not due to bone metastases.

Bronchioloalveolar Carcinoma

This is a subtype of adenocarcinoma that is not related to cigarette smoking. In its early stages it lines the alveolar membrane with a thin layer of tumor cells without destroying the alveolar architecture. Bronchioloalveolar carcinoma (BAC) can present as an isolated peripheral lesion, as multifocal disease

(often in both lungs), or as pan-lobar disease (sometimes with production of enormous quantities of mucous). It is the tumor most often identified in low-dose CT scan screening studies and has >90% 5-year survival if treated early, but behaves similar to adenocarcinoma in more advanced stages. Because of its low potential to spread outside of the lungs, multifocal BAC may be treated by lung transplantation in selected cases [75].

Large-Cell Undifferentiated Carcinoma

This is the least common of the NSCLCs. They tend to present as large, often cavitating, peripheral tumors. Their rapid growth rate may lead to widespread metastases, similar to adenocarcinoma.

Small-Cell Lung Cancer

This tumor of neuroendocrine origin is considered metastatic on presentation and is usually regarded as a medical, not a surgical disease [76]. The staging system differs from NSCLC and is divided simply into limited stage and extensive stage. Limited disease is defined as disease confined to one hemithorax that may be encompassed by one radiotherapy field. Treatment of limited stage SCLC with combination chemotherapy (etoposide/cisplatin or cyclophosphamide/doxorubicin/vincristine) gives objective response rates in over 80% of patients. In addition, these patients typically receive radical radiotherapy to the primary lung tumor and prophylactic cranial irradiation. Despite this initial response, the tumor invariably recurs and is quite resistant to further treatment. The overall survival rate is no better than 10%. Extensive stage disease is treated with chemotherapy and palliative radiation as needed.

There are two situations in which surgery for SCLC might be considered. The rare instance in which a solitary pulmonary nodule is diagnosed as SCLC, should be treated with surgical resection followed by chemotherapy. Salvage resection of a residual mass following chemotherapy for limited stage disease may offer some long-term survival in selected cases. Many of these patients will have mixed SCLC/NSCLC in which the small cell component has responded to chemotherapy and the non-small cell component is then resected. Also, patients with treated SCLC have an increased rate of second primary lung cancers, usually non-small cell lung cancer.

SCLC is known to cause a variety of paraneoplastic syndromes due to the production of peptide hormones and antibodies. The commonest of these is hyponatremia, usually due to an inappropriate production of antidiuretic hormone (SIADH). Cushing's syndrome and hypercortisolism through ectopic production of adrenocorticotrophic hormone (ACTH) are also commonly seen.

A well known but rare neurologic paraneoplastic syndrome associated with small-cell lung tumors is the Lambert-Eaton myasthenic syndrome due to impaired release of acetylcholine from nerve terminals. This typically presents as proximal

lower limb weakness and fatigability that may temporarily improve with exercise. The diagnosis is confirmed by electromyography (EMG) showing increasing amplitude of unusual action potentials with high-frequency stimulation and by serum antibodies. Similar to true myasthenia gravis patients (see Chap. 15), myasthenic syndrome patients are extremely sensitive to nondepolarizing muscle relaxants. However, unlike true myasthenics, they respond poorly to anticholinesterase reversal agents [77]. Clinical differences between myasthenia and the myasthenic syndrome are discussed in Chap. 15 [78]. Diaminopyridine has been reported to be useful both as a maintenance medication and to reverse residual postoperative neuromuscular blockade in these patients [79]. Other treatments of the Lambert-Eaton syndrome include: plasmapheresis, immunoglobulin, and guanidine. It is important to realize that there may be subclinical involvement of the diaphragm and muscles of respiration. TEA has been used following thoracotomy in these patients without complication. These patients' neuromuscular function may improve following resection of the lung cancer. A patient with a lung cancer and unusual symptoms of weakness should be referred to a Neurologist to rule out myasthenic syndrome. Nondepolarizing muscle relaxants should be avoided during anesthesia in these patients.

Carcinoid Tumors

Carcinoid tumors are low grade neuroendocrine malignancies and may be typical or atypical. Typical carcinoid tumors are most commonly found in the central airways and may present with obstructive symptoms or hemoptysis. Bronchoscopic biopsy or resection may cause significant bleeding. Five-year survival following resection for typical carcinoid exceeds 90%. Lymph node metastases are not as common as systemic metastasis. The carcinoid syndrome, which is caused by the ectopic synthesis of vasoactive mediators, is usually seen with carcinoid tumors of gut origin that have metastasized to the liver or rarely large primary pulmonary carcinoid tumors. Atypical carcinoid tumors are more often peripheral and are more aggressive and have a reduced survival rate. They often metastasize both regionally and systemically. Perioperative management of intrathoracic atypical carcinoid tumors is discussed in Chap. 15. These tumors can precipitate an intraoperative hemodynamic crisis or coronary artery spasm even during bronchoscopic resection [80]. The anesthesiologist should be prepared to deal with severe hypotension that may not respond to the usual vasoconstrictors and will require the use of the specific antagonists Octreotide or Somatostatin [81].

Pleural Tumors

Solitary fibrous tumors of pleura are usually large, space occupying masses that are usually attached to visceral pleura. They can be either benign or malignant, but most are easily resected with good results.

MPMs are strongly associated with exposure to asbestos fibers. Their incidence in Canada has almost doubled in the past 15 years. With the phasing out of asbestos-containing products and the long latent period between exposure and diagnosis, the peak incidence is not predicted for another 10–20 years. The tumor initially proliferates within the visceral and parietal pleura, typically forming a bloody effusion. Patients present with shortness of breath or dyspnea on exertion, dry cough or pain. Thoracentesis often relieves the symptoms but rarely provides a diagnosis. Pleural biopsy by video-assisted thoracoscopy is most efficient way to secure a diagnosis and talc poudrage is performed under the same anesthetic to treat the effusion.

MPMs respond poorly to therapy and the median survival is less than one year. In patients with very early disease, extrapleural pneumonectomy may be considered but it is difficult to know whether survival is improved. Recently, several groups have reported improved results with combinations of radiation, chemotherapy, and surgery. Extrapleural pneumonectomy is an extensive procedure that is rife with potential complications, both intra- and postoperative [82]. Blood loss from the denuded chest wall or major vascular structures is always a risk. Complications related to resection of diaphragm and pericardium are additional added risks to that of the pneumonectomy. Perioperative management for extrapleural pneumonectomy is discussed in Chap. 28.

Preoperative Assessment of the Patient with Lung Cancer

At the time of initial assessment, cancer patients should be assessed for the “4-M’s” associated with malignancy (Table 2.9): mass effects, metabolic abnormalities, metastases, and medications. The prior use of medications which can exacerbate oxygen-induced pulmonary toxicity such as bleomycin, should be considered [83]. Bleomycin is not used to treat primary lung cancers but patients presenting for excision of lung metastases from germ-cell tumors will often have received prior bleomycin therapy. Although the association between previous bleomycin therapy and pulmonary toxicity from high inspired oxygen concentrations is well documented, none of the details of the association are understood (i.e., safe doses of oxygen or safe period after bleomycin exposure). The safest anesthetic

TABLE 2.9. Anesthetic considerations in lung cancer patients (the “4 M’s”).

Mass effects: obstructive pneumonia, lung abscess, SVC syndrome, tracheobronchial distortion, Pancoast’s syndrome, recurrent laryngeal nerve or phrenic nerve paresis, chest wall or mediastinal extension
Metabolic effects: Lambert–Eaton syndrome, hypercalcemia, hypotremia, Cushing’s syndrome
Metastases: particularly to brain, bone, liver, and adrenal
Medications: chemotherapy agents, pulmonary toxicity (Bleomycin, Mitomycin), cardiac toxicity (Doxorubicin), renal toxicity (Cisplatin)

management is to use the lowest FiO_2 consistent with patient safety and to closely monitor oximetry in any patient who has received bleomycin. We have seen lung cancer patients who received preoperative chemotherapy with cisplatin, which is mildly nephrotoxic, and then developed an elevation of serum creatinine when they received NSAIDs postoperatively. For this reason, we do not routinely administer NSAIDs to patients who have been treated recently with cisplatin.

Postoperative Analgesia

The strategy for postoperative analgesia should be developed and discussed with the patient during the initial preoperative assessment; a full discussion of postoperative analgesia is presented in Chap. 46. Many techniques have been shown to be superior to the use of on-demand parenteral (intramuscular or intravenous) opioids alone in terms of pain control [84]. These include the addition of neuraxial blockade, intercostal/paravertebral blocks, interpleural local anesthetics, NSAIDs, etc. to narcotic based analgesia. Only epidural techniques have been shown to consistently have the capability to decrease post-thoracotomy respiratory complications [85, 86]. It is becoming more evident that TEA is superior to lumbar epidural analgesia. This seems to be due to the synergy which local anesthetics have with opioids in producing neuraxial analgesia. Studies suggest that epidural local anesthetics increase segmental bioavailability of opioids in the cerebrospinal fluid [87] and also that they increase the binding of opioids by spinal cord receptors [88]. Although lumbar epidural opioids can produce similar levels of post-thoracotomy pain control at rest, only the segmental effects of thoracic epidural local anesthetic and opioid combinations can reliably produce increased analgesia with movement and increased respiratory function following a chest incision [89, 90]. In patients with coronary artery disease, thoracic epidural local anesthetics seem to reduce myocardial oxygen demand and supply in proportion [91].

It is at the time of initial preanesthetic assessment that the risks and benefits of the various forms of post-thoracotomy analgesia should be explained to the patient. Potential contraindications to specific methods of analgesia should be determined such as coagulation problems, sepsis, or neurologic disorders. When it is not possible to place a thoracic epidural due to problems with patient consent or other contraindications, a reasonable second choice for analgesia is a paravertebral infusion of local anesthetic via a catheter placed intraoperatively in the open hemithorax by the surgeon [92]. This is combined with intravenous patient controlled opioid analgesia and NSAIDS whenever possible.

If the patient is to receive prophylactic anticoagulants and it is elected to use epidural analgesia, appropriate timing of anticoagulant administration and neuraxial catheter placement need to be arranged. ASRA guidelines suggest an interval of 2–4 h before or 1 h after catheter placement for prophylactic

heparin administration [93]. Low molecular weight heparin (LMWH) precautions are less clear, an interval of 12–24 h before and 24 h after catheter placement is recommended.

Premedication

Premedication should be discussed and ordered at the time of the initial preoperative visit. The most important aspect of preoperative medication is to avoid inadvertent withdrawal of those drugs which are taken for concurrent medical conditions (bronchodilators, antihypertensives, β -blockers, etc.). For some types of thoracic surgery, such as esophageal reflux surgery, oral antacid and/or H_2 -blockers or proton-pump inhibitors are routinely ordered preoperatively. We do not routinely order preoperative sedation or analgesia for pulmonary resection patients. Mild sedation such as an intravenous short acting benzodiazepine is often given immediately prior to placement of invasive monitoring lines and catheters. In patients with copious secretions, an antisialogogue (such as glycopyrrolate) is useful to facilitate fiberoptic bronchoscopy for positioning of a double-lumen tube or bronchial blocker. To avoid an intramuscular injection this can be given orally or intravenously immediately after placement of the intravenous catheter. It is a common practice to use short-term intravenous antibacterial prophylaxis such as a cephalosporin in thoracic surgical patients. If it is the local practice to administer these drugs prior to admission to the operating room they will have to be ordered preoperatively. Consideration for those patients allergic to cephalosporins or penicillin will have to be made at the time of the initial preoperative visit.

Initial Preoperative Assessment

The anesthetic considerations which should be addressed at the time of the initial preoperative assessment are summarized in Table 2.10. Patients need to be specifically assessed for risk factors associated with respiratory complications, which are the major cause of morbidity and mortality following thoracic surgery. Risk factors which can be modified preoperatively are listed in Table 2.11 [94].

TABLE 2.10. Initial preanesthetic assessment for thoracic surgery.

For all patients: assess exercise tolerance, simple spirometry: estimate ppoFEV1%, discuss postoperative analgesia, smoking cessation
Patients with ppoFEV1 <40%: full pulmonary function testing to include DLCO, Ventilation/perfusion lung scan if possible pneumonectomy, exercise testing
Cancer patients: consider the “4 M’s”: mass effects, metabolic effects, metastases, and medications
COPD patients: physiotherapy, bronchodilators, arterial blood gas if moderate or severe COPD
Increased renal risk: measure creatinine

TABLE 2.11. Probability for preoperative interventions to reduce the risk of pulmonary complications.

Risk factor	Intervention	Probability
Smoking	Cessation >8 weeks	++++
	Cessation <8 weeks	+
Exacerbation of COPD or asthma	Steroids, bronchodilators, and delay elective surgery	++++
	Antibiotics indicated by sputum	+++
Stable COPD or asthma	Physiotherapy	++++
	Bronchodilators	+++
	Rehabilitation	++
Obesity	Physiotherapy	++++
	Weight loss	++
Malnutrition	Oral nutrition program	++

++++=Multiple studies confirming; +++=both some data plus physiologic rationale supporting; ++=either some data or good physiologic rationale; + = limited data or physiologic rationale

Based on data from Liu and Mulroy [93]

TABLE 2.12. Final preanesthetic assessment for thoracic surgery.

Review initial assessment and test results
Assess difficulty of lung isolation: examine preoperative chest imaging
Assess risk of hypoxemia during one-lung ventilation

Final Preoperative Assessment

The final preoperative anesthetic assessment for the majority of thoracic surgical patients is carried out immediately prior to admission of the patient to the operating room. At this time it is important to review the data from the initial pre-thoracotomy assessment and the results of tests ordered at that time. In addition, two other specific areas affecting thoracic anesthesia need to be assessed: the potential for difficult lung isolation and the risk of desaturation during one-lung ventilation (Table 2.12).

Difficult Endobronchial Intubation

Anesthesiologists are familiar with the clinical assessment of the upper airway for ease of endotracheal intubation. In a similar fashion, each thoracic surgical patient must be assessed for the ease of endobronchial intubation. At the time of the preoperative visit, there may be historical factors or physical findings which lead to suspicion of difficult endobronchial intubation (previous radiotherapy, infection, previous pulmonary or airway surgery). In addition, there may be a written bronchoscopy report with a detailed description of anatomical features. The most useful predictor of difficult endobronchial intubation is the plain chest X-ray (Fig. 2.19).

The anesthesiologist should view the chest imaging him/herself prior to induction of anesthesia since neither the Radiologist's nor the Surgeon's report of the X-ray is made with the specific consideration of lung isolation in mind. A large portion of thoracic surgical patients will also have had a chest CT-scan done preoperatively. As anesthesiologists have learned to assess

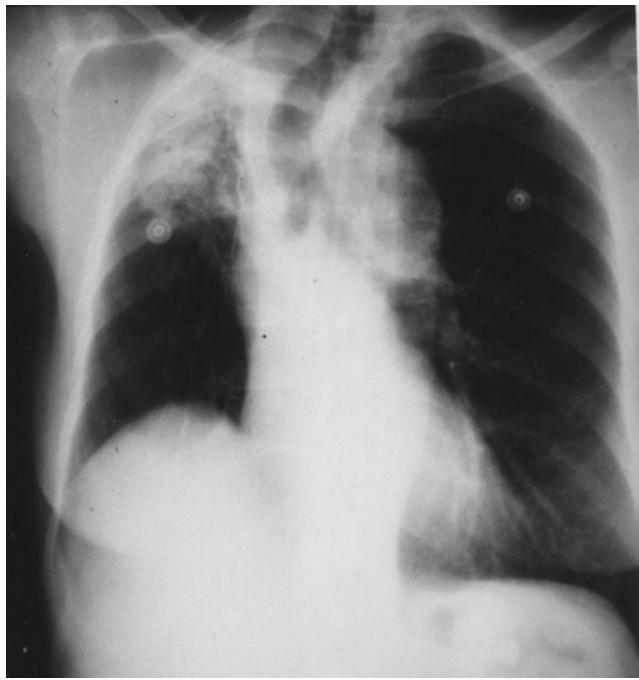


FIG. 2.19. Preoperative chest X-ray of a patient with a history of previous tuberculosis, right upper lobectomy, and recent hemoptysis presenting for right thoracotomy possible completion pneumonectomy. The potential problems positioning a left-sided double-lumen tube in this patient are easily appreciated by viewing the X-ray but are not mentioned in the Radiologist's report. The Anesthesiologist must examine the chest imaging him/herself preoperatively to anticipate problems in lung isolation.

X-rays for potential lung isolation difficulties, it is also worthwhile to learn to examine the CT-scan. Distal airway problems not detectable on the plain chest film can sometimes be visualized on the CT-scan: a side-to-side compression of the distal trachea, the so called "saber-sheath" trachea can cause obstruction of the tracheal lumen of a left-sided double-lumen tube during ventilation of the dependent (right) lung for a left thoracotomy [95]. Similarly, extrinsic compression or intra-luminal obstruction of a mainstem bronchus which can interfere with endobronchial tube placement may only be evident on the CT-scan. The major factors in successful lower airway management are anticipation and preparation based on the preoperative assessment. Management of lung isolation in patients with difficult upper and lower airways is discussed in Chap. 17.

Prediction of Desaturation During One-Lung Ventilation

In the vast majority of cases it is possible to identify preoperatively those patients which are most at risk of desaturation during one-lung ventilation (OLV) for thoracic surgery. The factors which correlate with desaturation during OLV are listed in Table 2.13. In patients at high-risk of desaturation, prophylactic measures can be used during OLV to decrease

TABLE 2.13. Factors which correlate with an increased risk of desaturation during one-lung ventilation.

High percentage of ventilation or perfusion to the operative lung on preoperative <i>V/Q</i> scan
Poor PaO_2 during two-lung ventilation, particularly in the lateral position intraoperatively
Right-sided thoracotomy
Normal preoperative spirometry (FEV1 or FVC) or restrictive lung disease
Supine position during one-lung ventilation

this risk. The most useful prophylactic measures are the use of continuous positive airway pressure (CPAP) 2–5 cm H₂O of oxygen to the non-ventilated lung and/or positive end-expiratory pressure (PEEP) to the dependent lung.

The most important predictor of PaO_2 during OLV is the PaO_2 during two-lung ventilation, specifically the intraoperative PaO_2 during two-lung ventilation in the lateral position prior to OLV [96]. The proportion of perfusion or ventilation to the nonoperated lung on preoperative *V/Q* scans also correlates with the PaO_2 during OLV [97]. If the operative lung has little perfusion preoperatively due to unilateral disease, the patient is unlikely to desaturate during OLV. The side of the thoracotomy has an effect on PaO_2 during OLV. The left lung being 10% smaller than the right, there is less shunt when the left lung is collapsed. In a series of patients, the mean PaO_2 during left thoracotomy was approximately 70 mmHg higher than during right thoracotomy [98]. Finally, the degree of obstructive lung disease correlates in an inverse fashion with PaO_2 during OLV. Other factors being equal, patients with more severe airflow limitation on preoperative spirometry will tend to have a better PaO_2 during OLV than patients with normal spirometry (see Chap. 6) [99].

Assessment for Repeat Thoracic Surgery

Patients who survive lung cancer surgery form a high-risk cohort to have a recurrence of the original tumor or to develop a second primary. The incidence of developing a second primary lung tumor is estimated at 2%/year. The use of routine postoperative follow-up screening with low-dose spiral CT scans will probably increase the rate of early detection of recurrent or repeat primary tumors [100]. Patients who present for repeat thoracotomy should be assessed using the same framework as those who present for surgery the first time. Predicted values for postoperative respiratory function based on the preoperative lung mechanics, parenchymal function, exercise tolerance, and the amount of functioning lung tissue resected should be calculated and used to identify patients at increased risk.

Clinical Case Discussion

Case: A 65-year-old male presents for anesthesia preoperative assessment (Fig. 2.20). He is scheduled for a bronchoscopy/mediastinoscopy and right pneumonectomy. He is a smoker who presented to his family doctor 2 weeks ago after minor



FIG. 2.20. Chest X-ray of a 65-year-old male, with carcinoma involving the right middle and lower lobes, being assessed for possible right pneumonectomy.

hemoptysis. He has no significant known comorbidities and past history is otherwise unremarkable. A fine needle biopsy has confirmed the diagnosis of non-SCLC. The anesthesia team will need to decide if the patient will tolerate the proposed procedure and if so, then what management strategies can be used to improve the perioperative outcome.

Questions: apart from routine preoperative assessment for major surgery:

What pulmonary function evaluation is indicated?

What cardiac investigations are indicated?

What specific anesthetic considerations are related to the patient's lung cancer?

What other system function should be documented?

Pulmonary function evaluation: lung mechanical function (spirometry: FEV1), pulmonary parenchymal function (DLCO), exercise capacity, and ventilation/perfusion scan (see Sect. "Assessment of Respiratory Function").

Cardiac evaluation: ECG (echocardiography and stress testing not indicated) (see Sect. "Cardiovascular Disease").

Considerations related to lung cancer: tumor mass effects, metabolic (paraneoplastic) effects, metastases, and adjuvant medications

Other systems: renal function

Will the patient tolerate the procedure?

Results of investigations: FEV1 65%, DLCO 70%, exercise tolerance: the patient can climb four flights of stairs without stopping. V/Q scan R/L 40/60 for both V and Q . Other investigations are all within normal limits.

Predicted postoperative (ppo) FEV1 and DLCO will be in the range of 30–35% and adjusted for the V/Q scan possibly higher. These indicate increased risk but acceptable

survival given the patient's age <70. A bilobectomy could be considered for elderly or high-risk patients (see Sect. "Age").

What management strategies will improve the patient's outcome?

Smoking cessation.

Pre- and postoperative chest physiotherapy.

TEA has not been clearly proven to improve outcomes in patients with normal pulmonary function, but does improve function in moderate and severe COPD. This patient's risk of respiratory complications may be improved by either thoracic epidural or paravertebral analgesia (see also Chap. 46).

Moderate perioperative fluid restriction and lung-protective ventilation are associated with a decreased risk of postoperative acute lung injury particularly after pneumonectomy (see also Chap. 10).

Calcium channel blockers may be associated with a decreased risk of postoperative atrial fibrillation (see also Chap. 44).

Preoperative β -blockade, statins, or α -2 blockers are not proven to decrease cardiac ischemic risks in this patient at low risk of perioperative ischemia.

References

1. Slinger PD, Johnston MR. Preoperative assessment: an anesthesiologist's perspective. *Thorac Surg Clin*. 2005;15:11–26.
2. Licker M, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg*. 2006;81:1830–8.
3. Wright CD, Gaisert HA, Grab JD, et al. Predictors of prolonged post-operative length of stay after lobectomy for lung cancer. *Ann Thorac Surg*. 2008;85:1857–65.
4. Culver BH. Preoperative assessment of the thoracic surgery patient: pulmonary function testing. *Semin Thorac Cardiovasc Surg*. 2001;13:92–104.
5. British Thoracic Society. Guidelines on the selection of patients with lung cancer for surgery. *Thorax*. 2001;56:89–108.
6. Nakahara K, Ohno K, Hashimoto J, et al. Prediction of postoperative respiratory failure in patients undergoing lung resection for cancer. *Ann Thorac Surg*. 1988;46:549–54.
7. Cerfolio RJ, Allen MS, Trastak VF, et al. Lung resection in patients with compromised pulmonary function. *Ann Thorac Surg*. 1996;62:348–51.
8. Win T, Jackson A, Sharples L, et al. Relationship between pulmonary function and lung cancer surgical outcome. *Eur Respir J*. 2005;25:594–9.
9. Linden PA, Bueno R, Colson YL, et al. Lung resection in patients with $FEV1 < 35\%$ predicted. *Chest*. 2005;127:1984–90.
10. Bach PB, Cramer LD, Schrag D. The influence of hospital volume on survival after resection for lung cancer. *N Engl J Med*. 2001;345:181–8.
11. Brunelli A, Rocco G. Spirometry: predicting outcome and risk. *Thorac Surg Clin*. 2008;18:1–8.
12. Slinger PD, Kruger M, McRae K, Winton T. The relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung ventilation. *Anesthesiology*. 2001;95:1096–102.

13. Ferguson MK, Vigneswaran WT. Diffusing capacity predicts morbidity after lung resection in patients without obstructive lung disease. *Ann Thorac Surg.* 2008;85:1158–65.
14. National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med.* 2003;348:2059.
15. Weisman IM. Cardiopulmonary exercise testing in the preoperative assessment for lung resection surgery. *Semin Thorac Cardiovasc Surg.* 2001;13:116–22.
16. Coyle EF. Improved muscular efficiency as Tour de France champion matures. *J Appl Physiol.* 2005;98:2191–6.
17. Walsh GL, Morice RC, Putnam JB, et al. Resection of lung cancer is justified in high risk patients selected by oxygen consumption. *Ann Thorac Surg.* 1994;58:704–10.
18. Nagamatsu Y, Shima I, Hayashi A, et al. Preoperative spirometry versus expired gas analysis during exercise testing as predictors of cardiopulmonary complications after lung resections. *Surg Today.* 2004;34:107–10.
19. Forshaw MJ, Strauss DC, Davies AR, et al. Is cardiopulmonary exercise testing a useful test before esophagectomy? *Ann Thorac Surg.* 2008;85:294–9.
20. Carter R, Holiday DB, Stocks J, et al. Predicting oxygen uptake for men and women with moderate to severe chronic obstructive pulmonary disease. *Arch Phys Med Rehabil.* 2003;84:1158–64.
21. Ninan M, Sommers KE, Landranau RJ, et al. Standardized exercise oximetry predicts post-pneumonectomy outcome. *Ann Thorac Surg.* 1997;64:328–33.
22. Bolliger CT, Wyser C, Roser H, et al. Lung scanning and exercise testing for the prediction of postoperative performance in lung resection candidates at increased risk for complications. *Chest.* 1995;108:341–8.
23. Olsen GN, Bolton JWR, Weiman DS, Horning CA. Stair climbing as an exercise test to predict postoperative complications of lung resection. *Chest.* 1991;99:587–90.
24. Kinasewitz GT, Welsh MH. A simple method to assess postoperative risk. *Chest.* 2001;120:1057–8.
25. Heerd PM. Post-thoracotomy cardiovascular adaptations and complications. In: Kaplan J, Slinger P, editors. *Thoracic anaesthesia.* 3rd ed. Philadelphia, PA: Churchill Livingston; 2003. p. 423–35.
26. Koegelenberg CFN, Bollinger CT. Assessing regional lung function. *Thorac Surg Clin.* 2008;18:19–29.
27. Win T, Larouche CM, Groves AM, et al. Use of quantitative lung scintigraphy to predict pulmonary function in lung cancer patients undergoing lobectomy. *Ann Thorac Surg.* 2004;78:1215–9.
28. Wu MT, Pan HB, Chiang AA, et al. Predicting postoperative lung function in patients with lung cancer. *AJR Am J Roentgenol.* 2002;178:667–72.
29. Ohno Y, Koyama H, Nogami M, et al. Post-operative lung function in lung cancer patients: comparative analysis of predictive capacity of MRI, CT, SPECT. *AJR Am J Roentgenol.* 2007;189:400–8.
30. Tisi GM. Preoperative evaluation of pulmonary function. *Am Rev Respir Dis.* 1979;119:293–301.
31. Lewis Jr JW, Bastanfar M, Gabriel F, Mascha E. Right heart function and prediction of respiratory morbidity in patients undergoing pneumonectomy with moderately severe cardiopulmonary dysfunction. *J Thorac Cardiovasc Surg.* 1994;108:169–75.
32. Amar D, Burt M, Roistacher N, Reinsel RA, Ginsberg RJ, Wilson R. Value of perioperative echocardiography in patients undergoing major lung resection. *Ann Thorac Surg.* 1996;61:516–22.
33. Jordan S, Evans TW. Predicting the need for intensive care following lung resection. *Thorac Surg Clin.* 2008;18:61–9.
34. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol.* 2007;50:1707–32.
35. von Knorring J, Lepäntalo M, Lindgren L, Lindfors O. Cardiac arrhythmias and myocardial ischemia after thoracotomy for lung cancer. *Ann Thorac Surg.* 1992;53:642–7.
36. Etchells E, Meade M, Tomlinson G, et al. Semiquantitative dipyridamole myocardial stress perfusion imaging before noncardiac vascular surgery: a metaanalysis. *J Vasc Surg.* 2002;36:534–40.
37. Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and treatment of coronary artery disease: systematic review and meta-analysis. *Heart.* 2008;94:1386–93.
38. Brett AS. Are the current perioperative risk management strategies flawed? *Circulation.* 2008;117:3145–51.
39. Yang H, Beattie WS. POISE results and perioperative β -blockade. *Can J Anaesth.* 2008;55:727–34.
40. ASA Committee on Standards and Practice Parameters. Practice alert for the perioperative management of patients with coronary artery stents. *Anesthesiology.* 2009;110:22–3.
41. Ritchie AJ, Bowe P, Gibbons JRP. Prophylactic digitalisation for thoracotomy: a reassessment. *Ann Thorac Surg.* 1990;50: 86–8.
42. de Perrot M, Mcrae K, Anraku M, et al. Risk factors for major complications after extra-pleural pneumonectomy for malignant pleural mesothelioma. *Ann Thorac Surg.* 2008;85:1206–10.
43. Boldt J, Muller M, Uphus D, et al. Cardio-respiratory changes in patients undergoing pulmonary resection using different anesthetic management techniques. *J Cardiothorac Vasc Anesth.* 1996;10:854–7.
44. Sekine Y, Kesler KA, Behnia M, et al. COPD may increase the incidence of refractory supraventricular arrhythmias following pulmonary resection for non-small cell lung cancer. *Chest.* 2001;120:1783–90.
45. Amar D, Roistacher N, Rusch VW. Effects of diltiazem prophylaxis on the incidence and clinical outcome of atrial arrhythmias after thoracic surgery. *J Thorac Cardiovasc Surg.* 2000;120:790–8.
46. Lindgren L, Lepäntalo M, Von Knorring J, et al. Effect of verapamil on right ventricular pressure and atrial tachyarrhythmia after thoracotomy. *Br J Anaesth.* 1991;66:205–11.
47. Oka T, Ozawa Y, Ohkubo Y. Thoracic epidural bupivacaine attenuates supraventricular tachyarrhythmias after pulmonary resection. *Anesth Analg.* 2001;93:253–9.
48. Osaki T, Shirakusa T, Kodate M, et al. Surgical treatment of lung cancer in the octogenarian. *Ann Thorac Surg.* 1994;57:188–92.
49. Brunelli A, Monteverde M, Al Refai M. Stair climbing as a predictor of cardiopulmonary complications after pulmonary lobectomy in the elderly. *Ann Thorac Surg.* 2004;77:266–70.
50. Spaggiari L, Scanagatta P. Surgery of non-small cell lung cancer in the elderly. *Curr Opin Oncol.* 2007;19:84–91.
51. Golledge J, Goldstraw P. Renal impairment after thoracotomy: incidence, risk factors and significance. *Ann Thorac Surg.* 1994;58:524–8.

52. Slinger PD. Postpneumectomy pulmonary edema: good news, bad news. *Anesthesiology*. 2006;105:2–5.
53. Cywinski JB, Xu M, Sessler DI, et al. Predictors of prolonged postoperative endotracheal intubation in patients undergoing thoracotomy for lung resection. *J Cardiothorac Vasc Anesth*. 2009;6:766–9.
54. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1995;152:s77–121.
55. Parot S, Saunier C, Gauthier H, Milic-Emile J, Sadoul P. Breathing pattern and hypercapnia in patients with obstructive pulmonary disease. *Am Rev Respir Dis*. 1980;121:985–91.
56. Aubier M, Murciano D, Milic-Emili J, et al. Effects of the administration of O₂ on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. *Am Rev Respir Dis*. 1980;122:747–54.
57. Simpson SQ. Oxygen-induced acute hypercapnia in chronic obstructive pulmonary disease: what's the problem? *Crit Care Med*. 2002;30:258–9.
58. Hanson III CW, Marshall BE, Frasch HF, Marshall C. Causes of hypercarbia in patients with chronic obstructive pulmonary disease. *Crit Care Med*. 1996;24:23–8.
59. Nguyen DM, Mulder DS, Shennib H. Altered cellular immune function in atelectatic lung. *Ann Thorac Surg*. 1991;51:76–80.
60. Hublitz UF, Shapiro JH. Atypical pulmonary patterns of congestive failure in chronic lung disease. *Radiology*. 1969;93:995–1006.
61. Sasaki F, Ishizaki T, Mifune J, et al. Bronchial hyperresponsiveness in patients with chronic congestive heart failure. *Chest*. 1990;97:534–8.
62. Nisar M, Earis JE, Pearson MG, Calverly PMA. Acute bronchodilator trials in chronic obstructive pulmonary disease. *Am Rev Respir Dis*. 1992;146:555–9.
63. Warner DO. Preventing postoperative pulmonary complications. *Anesthesiology*. 2000;92:1467–72.
64. Cesario A, Ferri L, Cardaci V, et al. Pre-operative pulmonary rehabilitation and surgery for lung cancer. *Lung Cancer*. 2007;57:118–9.
65. Nici L. Preoperative and postoperative pulmonary rehabilitation in lung cancer patients. *Thorac Surg Clin*. 2008;18:39–43.
66. Benzo RP. Pulmonary rehabilitation in lung cancer. *J Cardiolpulm Rehabil Prev*. 2007;27:61–4.
67. Vaporciyan AA, Merriman KW, Ece F, et al. Incidence of major pulmonary complications after pneumonectomy; association with timing of smoking cessation. *Ann Thorac Surg*. 2002;73:420–5.
68. Akrawi W, Benumof JL. A pathophysiological basis for informed preoperative smoking cessation counseling. *J Cardiothorac Vasc Anesth*. 1997;11:629–40.
69. Moller A, Tonnesen H. Risk reduction: perioperative smoking intervention. *Best Pract Res Clin Anaesthesiol*. 2006;20:237–48.
70. Barrera R, Shi W, Amar D, et al. Smoking and timing of cessation. Impact on pulmonary complications after thoracotomy. *Chest*. 2005;127:1977–83.
71. Warner DO. Feasibility of tobacco interventions in anesthesiology practices: a pilot study. *Anesthesiology*. 2009;110:1223–8.
72. Farjah F, Wood DE, Yanez III D, et al. Temporal trends in the management of potentially resectable lung cancer. *Ann Thorac Surg*. 2008;85:1850–6.
73. National Health Statistics of the United States 2007. www.cancer.org.
74. Feinstein MB, Bach PB. Epidemiology of lung cancer in lung cancer: past, present and future. *Chest Surg Clin*. 2000;10:653–61.
75. de Perrot M, Cherenko S, Waddell T, et al. Role of lung transplantation in the treatment of bronchogenic carcinomas for patients with end-stage pulmonary disease. *J Clin Oncol*. 2004;22:4351–6.
76. Johnson BE. Management of small cell lung cancer. *Clin Chest Med*. 1993;14:173–87.
77. Levin KH. Paraneoplastic neuromuscular syndromes. *Neurol Clin*. 1997;15:597–614.
78. Petty R. Lambert–Eaton myasthenic syndrome. *Pract Neurol*. 2007;7:265–7.
79. Telford RJ, Holloway TE. The myasthenic syndrome: anesthesia in a patient treated with 3–4 diaminopyridine. *Br J Anaesth*. 1990;64:363–6.
80. Mehta AC, Rafanan AL, Bulkley R, et al. Coronary spasm and cardiac arrest from carcinoid syndrome during laser bronchoscopy. *Chest*. 1999;115:598–600.
81. Vaughan DJ, Brunner MD. Anesthesia for patients with the carcinoid syndrome. *Int Anesthesiol Clin*. 1997;35:129–42.
82. Hartigan PM, Ng JM. Anesthetic strategies for patients undergoing extrapleural pneumonectomy. *Thorac Surg Clin*. 2004;14:575–83.
83. Sleijfer S. Bleomycin-induced pneumonitis. *Chest*. 2001;120:617–24.
84. Kavanagh BP, Katz J, Sandler AN. Pain control after thoracic surgery: a review of current techniques. *Anesthesiology*. 1994;81:737–59.
85. Licker M, de Perrot M, Hohn L, et al. Perioperative mortality and major cardio-pulmonary complications after lung surgery for non-small cell carcinoma. *Eur J Cardiothorac Surg*. 1999;15:314–9.
86. Rigg JRA, Jamrozik K, Myles PS. Epidural anaesthesia and analgesia and outcome of major surgery: a randomized trial. *Lancet*. 2005;359:1276–82.
87. Hansdottir V, Woestenborghs R, Nordberg G. The pharmacokinetics of continuous epidural sufentanil and bupivacaine infusion after thoracotomy. *Anesth Analg*. 1996;83:401–6.
88. Tejwani GA, Rattan AK, McDonald JS. Role of spinal opioid receptors in the antinociceptive interactions between intrathecal morphine and bupivacaine. *Anesth Analg*. 1992;74:726–34.
89. Hansdottir V, Bake B, Nordberg G. The analgesic efficiency and adverse effects of continuous epidural sufentanil and bupivacaine infusion after thoracotomy. *Anesth Analg*. 1996;83:394–400.
90. Bauer C, Hentz J-G, Ducrocq X, et al. Lung function after lobectomy: a randomized trial comparing thoracic epidural ropivacaine/sufentanil and intra-venous morphine for patient-controlled analgesia. *Anesth Analg*. 2007;105:238–44.
91. Saada M, Catoire P, Bonnet F, et al. Effect of thoracic epidural anesthesia combined with general anesthesia on segmental wall motion assessed by transesophageal echocardiography. *Anesth Analg*. 1992;75:329–35.
92. Karmakar MK. Thoracic paravertebral block. *Anesthesiology*. 2001;95:771–80.
93. Liu SS, Mulroy MF. Neuraxial anesthesia and analgesia in the presence of standard heparin. *Reg Anesth Pain Med*. 1998;23(6 Suppl 2):157–63.

94. Kempainen RR, Benditt JO. Evaluation and management of patients with pulmonary disease before thoracic and cardiovascular surgery. *Semin Thorac Cardiovasc Surg*. 2001;13:105–15.
95. Bayes J, Slater EM, Hadberg PS, Lawson D. Obstruction of a double-lumen tube by a saber-sheath trachea. *Anesth Analg*. 1994;79:186–8.
96. Slinger P, Suissa S, Triolet W. Predicting arterial oxygenation during one-lung anaesthesia. *Can J Anaesth*. 1992;39:1030–5.
97. Hurford WE, Kokar AC, Strauss HW. The use of ventilation/perfusion lung scans to predict oxygenation during one-lung anaesthesia. *Anesthesiology*. 1987;67:841–4.
98. Lewis JW, Serwin JP, Gabriel FS, Bastaufar M, Jacobsen G. The utility of a double-lumen tube for one-lung ventilation in a variety of non-cardiac thoracic surgical procedures. *J Cardiothorac Vasc Anesth*. 1992;6:705–10.
99. Katz JA, Lavern RG, Fairley HB, et al. Pulmonary oxygen exchange during endobronchial anesthesia, effect of tidal volume and PEEP. *Anesthesiology*. 1982;56:164–71.
100. Naunheim KS, Virgo KS. Postoperative surveillance following lung cancer resection. *Chest Surg Clin N Am*. 2001;11:213–25.
101. Patterson AG. Pearson's thoracic and esophageal surgery. 3rd ed. Philadelphia, PA: Elsevier; 2008. p. 1168.
102. Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, et al. A brief self-administered questionnaire to determine functional capacity (The Duke Activity Status Index). *Am J Cardiol*. 1989;15:651–4.
103. Ainsworth BE, Haskell WL, Leon AS, Jacobs Jr DR, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc*. 1993;25:71–80.
104. Goldstraw P, Crowley J, Chansky K, Girous DJ, Groome PA, Rami-Porta R, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. *J Thorac Oncol*. 2007;2:706–14.

3

Thoracic Imaging

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Key Points

- Radiological images play an important role during the evaluation of patients undergoing thoracic surgery.
- Radiological studies must be reviewed, including a posterior–anterior chest radiograph and computed tomography scan of the chest.
- Special emphasis should be given to mediastinal mass with compromise to the airway or great vessels by reviewing the computed tomography scan of the chest.
- Multidetector computed tomography (CT) scan and tracheobronchial reconstruction are more specific studies in the thoracic surgical patient, and allow measurements of the airway.
- Magnetic resonance imaging (MRI) provides greater contrast resolution than CT scans and offers the potential for tissue characterization. An MRI is indicated in selected cases, i.e., mediastinal mass with invasion of the superior vena cava.

Introduction

Radiological images play an important role in the preoperative, intraoperative and postoperative evaluation, and diagnosis of patients undergoing thoracic surgery. During the preoperative visit evaluation of the thoracic surgical patient, the clinician

must have an understanding of the disease and also become familiar with radiological studies to be able to identify abnormal airway anatomy or compromises to the airway or to use caliper measurements in the tracheobronchial tree if necessary when selecting lung isolation devices. Another important component to a successful preoperative evaluation is an understanding of normal tracheobronchial anatomy. This chapter will be focused on reviewing normal tracheobronchial anatomy and radiological images, with special interest for anesthesiologists involved in the care of the thoracic surgical patient.

Normal Tracheobronchial Anatomy

The trachea is a cartilaginous and fibromuscular structure that extends from the inferior aspect of the cricoid cartilage to the level of the carina [1]. The adult trachea is, on average, 15 cm long. The trachea is composed of 16–22 C-shaped cartilages. The cartilages compose the anterior and lateral walls of the trachea and are connected posteriorly by the membranous wall of the trachea, which lacks cartilage and is supported by the trachealis muscle.

The average diameter in a normal trachea is 22 mm in men and 19 mm in women. In men, the coronal diameter ranges from 13 to 22 mm and the sagittal diameter ranges from 13 to 27 mm. In women, the average coronal diameter is 10–21 mm and the sagittal is 10–23 mm [2]. The tracheal wall is about

3 mm in thickness in both men and women, with a tracheal lumen that is often ovoid shape.

The trachea is located in the midline position, but often can be deviated to the right at the level of the aortic arch, with a greater degree of displacement in the setting of an atherosclerotic aorta, advanced age or in the presence of severe chronic obstructive pulmonary disease (COPD). With COPD or aging, the lateral diameter of the trachea may decrease with a corresponding increase in the anteroposterior diameter. Conversely, COPD may also lead to softening of the tracheal rings with a decrease in the anteroposterior diameter of the trachea [3]. The cricoid cartilage is the narrowest part of the trachea with an average diameter of 17 mm in men and 13 mm in women.

The trachea bifurcates at the carina into the right and left mainstem bronchus. An important fact is that the tracheal lumen narrows slightly as it progresses towards the carina. The tracheal bifurcation is located at the level of the sternal angle anteriorly and the fifth thoracic vertebra posteriorly. The right mainstem bronchus continues as the bronchus intermedius after the take-off of the right upper lobe bronchus. In men, the average distance from the tracheal carina to the take-off of the right upper lobe bronchus is 2.0 cm, whereas it is approximately 1.5 cm in women. One in every 250 individuals from the general population may have an abnormal take-off of the right upper lobe bronchus emerging from above the tracheal carina on the right side [4]. The diameter of the right mainstem bronchus is an average of 17.5 mm in men and 14.0 mm in women. The trifurcation of the right upper lobe bronchus consists of the apical, anterior, and posterior divisions. The average distance from the tracheal carina to the bifurcation of the left upper and left lower lobe is approximately 5.0 cm in men and 4.5 cm in women. The left mainstem bronchus is longer than the right mainstem bronchus, and it divides into the left upper and the left lower lobe bronchus. The left upper lobe bronchus has a superior and inferior division [5].

Chest Radiographs

The most common study in the patient undergoing thoracic, esophageal, or cardiac surgery is the chest X-radiograph (X-ray). The standard routine chest radiography consists of an erect radiograph made in the posterior–anterior (PA) projection and a left lateral radiograph, both obtained at full inspiration. The normal chest cavity contains four radiographic densities that are easily identified: air, fat, water, and calcium and other metals including bones, granulomas, and vascular calcification. The lungs, which are mostly air and contain some water, blood vessels, bronchi, nerves, lymphatics, alveolar walls, and interstitial tissues, provide the natural contrast that is the basis of chest radiology. When evaluating a chest X-ray, the changes in these densities, which provide natural contrast, are what are observed.

Radiologists in general refer to two regions: the silhouette sign and summation. Depending on the part or parts of the lungs

that are involved, the result of this change in the absorption of X-rays is seen by the effect on the normal surface of a hemidiaphragm, for example, or if the descending aorta cannot be seen then this is an indication that an unusual amount of aerated lung no longer touches the anatomic part. This occurs in part because the alveolar spaces are wholly or partially filled with fluid usually blood, pus or water or in part because the lung has collapsed and decreased the normal ratio of air and soft tissue. The end result in the latter case would be an increase in opacity which is what the X-ray beam reveals. The heart border and the diaphragm are normally seen because of their interface with aerated lung. When the contiguous lung is not aerated, the opaque tissue of the affected lung blends visually with the soft tissue opacity of the heart and the heart border is no longer visible. This is what is termed the silhouette sign. Summation by definition is the result of superimposition of many layers of lung tissue, so that the final visual effect is that of a greater amount of tissue in the path of a particular part of the X-ray beam. This is observed when the opacity of fluid in the pleural space, interstitial space, or even lung parenchyma is added on the normal structure of the lung [6]. The most important skill for evaluating a chest X-ray is the knowledge of normal anatomic variants, specific patterns with pathological changes and the common signs of abnormal states. Lateral decubitus radiographs are commonly employed to determine the presence or mobility of pleural effusions. These views can also be obtained to detect small pneumothoraces, particularly in patients who are confined to bed and unable to sit or stand erect. A new generation of digital X-ray systems based on flat panel detections is now emerging and these provide good image quality and very rapid direct access to digital images.

Chest Radiographs and Pulmonary Disease

The basic underlying change in the chest film that allows the detection and diagnosis of abnormalities is usually due to an alteration in lung opacity. This can be caused by technical factors, physiologic variation, or pathologic mechanisms [7]. Diseases that affect the chest can usually be thought of as either those that make the film lighter (increase opacity) or those that make it darker (increase lucency).

For chest disease with increased opacity on radiographs, the conditions that are marked by focal or global increase in the opacity of the film are first examined. These conditions include: atelectasis, pulmonary edema, acute respiratory distress syndrome, etc.

Lung Mass and Chest X-Rays

Pulmonary neoplasia present as opacities on films although usually as a more focal area with varying contours. However, smaller lesions may be very difficult to visualize, particularly when there are overlying bones or other soft tissue. Figure 3.1a shows a posteroanterior chest radiograph on a 68-year-old

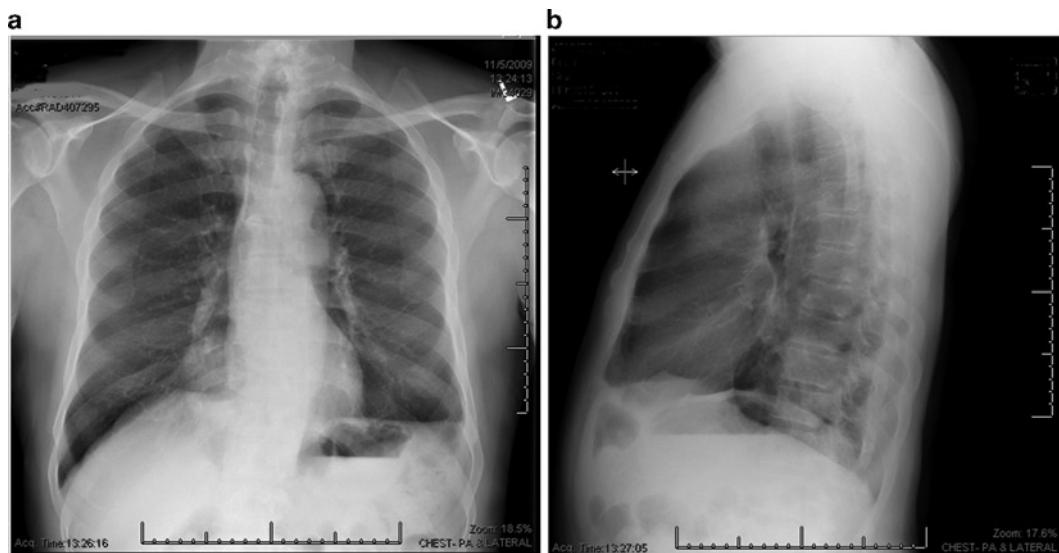


FIG. 3.1. (a) A posteroanterior chest radiograph of a 68-year-old male with a lung neoplasm of the right lower lobe. The mass is clearly visible between the eighth and ninth rib in the right hemithorax. (b) A lateral chest radiograph showing a round mass in the right hemithorax.

male with a lung neoplasm on the right lower lobe. The mass is clearly visible between the eighth and ninth rib on the right hemithorax. Figure 3.1b shows a lateral chest radiograph showing a round mass on the right hemithorax.

Mediastinal Mass and Chest X-Rays

In order to understand mediastinal masses and radiological images it is important to be familiar with the anatomy of the mediastinum. The mediastinum is situated between the two pleural cavities. It extends superiorly from the root of the neck and the thoracic inlet to the hemidiaphragm inferiorly. It is divided into the superior and inferior mediastinum by the transverse thoracic plane, which is an imaginary plane extending horizontally from the sternal angle anteriorly to the border of the fourth thoracic vertebra posteriorly. The inferior mediastinum is subdivided into anterior, middle, and posterior compartments. The anterior mediastinum contains the thymus, trachea, esophagus, vessels, and arteries as well as lymph nodes, any abnormal growth in this region will affect the adjacent area. A mass in this area may compress the tracheobronchial tree and/or major vessels (superior vena cava and pulmonary vessels). The middle mediastinum is the space occupied by the heart and pericardium [8, 9]. Figure 3.2a shows a schematic representation of mediastinal anatomy and Fig. 3.2b a lateral normal radiograph of the chest showing the potential location of mediastinal mass. A variety of neoplasms and other lesions present with anterior mediastinal involvement. Thymoma is the most common primary neoplasm of the anterior mediastinum [10].

Regarding radiological studies in patients with a suspected anterior mediastinal mass, the initial study generally is a standard biplane chest radiography, which will identify up to 97% of mediastinal tumors. The chest X-ray also provides important information regarding the size and the location of the mass [11].

In addition, in this patient group in particular, special attention must be paid to the lateral radiography of the chest to determine the overall extent of the mass and potential involvement of adjacent structures. A barium contrast esophagogram may help to determine whether there is esophageal or tracheobronchial involvement. Figure 3.3a shows an anterior mediastinal mass in the left hemithorax of the posteroanterior chest radiograph. Figure 3.3b shows a lateral radiograph with esophageal contrast where there is a mediastinal mass without compromise to the tracheobronchial tree.

Bullae

Emphysema is characterized by a permanent increase in air spaces distal to the terminal bronchiole beyond the normal size. There is destruction of tissue, leading to a loss of alveolar surface available to participate in air exchange and sometimes, severe displacement of the adjacent normal lung. Many of the cases of emphysema seen in adult patients are strongly associated with cigarette smoking. The most striking image in a patient with advanced emphysema is a marked hyperinflation with an increase in the anteroposterior diameter of the chest, flattening of the diaphragmatic surfaces, and a generalized increase in the blackness of the film. Also there is a change in the vascular pattern; with attenuated vessels thinned and spread apart.

Often bullous areas are noted as large thin-walled air cysts, especially the apices. A bulla is defined as an air-filled space 1 cm or greater in diameter within the lung parenchyma that forms as a result of this destructive process. Rarely, one or more bullae enlarge to such a degree that they occupy more than one-third of the hemithorax. The term giant bullae is then applied. These easily distensible reservoirs are preferentially filled during inspiration, causing the collapse of adjacent, more normal lung parenchyma [12, 13]. Figure 3.4a shows a patient with

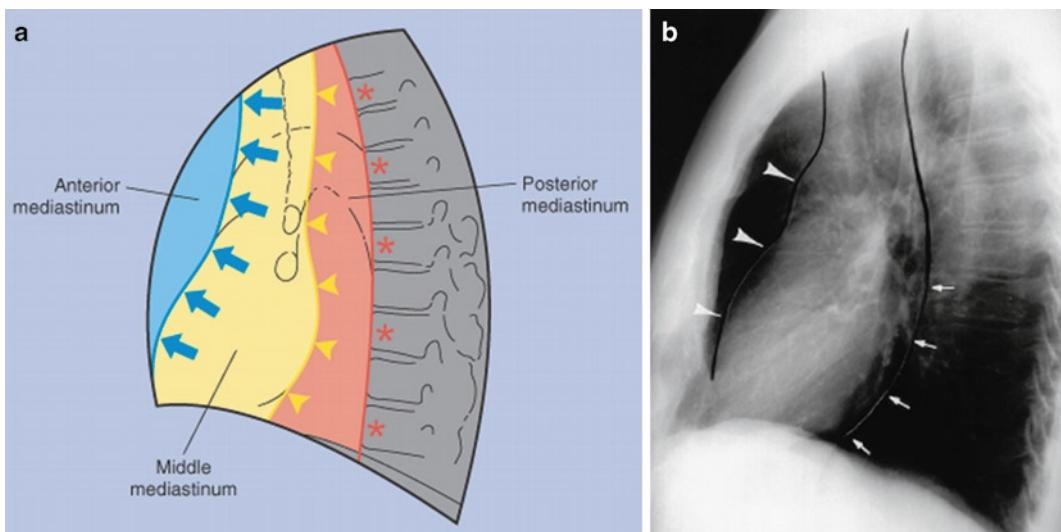


FIG. 3.2. (a) A schematic representation of mediastinal anatomy and (b) a lateral normal radiograph of the chest showing the potential location of a mediastinal mass. The arrows show the outline of the heart and great vessels.

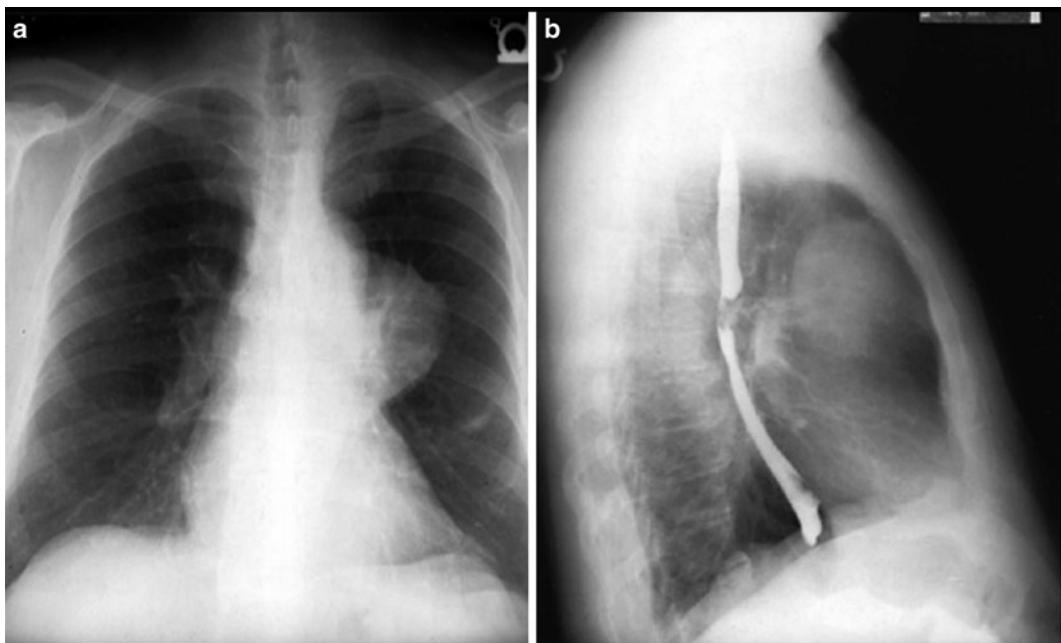


FIG. 3.3. (a) An anterior mediastinal mass in the left hemithorax of the posteroanterior chest radiograph. (b) A lateral radiograph with esophageal contrast where there is a mediastinal mass without compromise to the tracheobronchial tree.

emphysema and Fig. 3.4b shows a lateral chest radiograph of the same patient. Figure 3.5 shows a PA chest X-ray and lateral radiograph of a patient with bullae. Figure 3.6 displays the chest X-ray showing a giant bulla occupying more than two thirds of the right hemithorax and compressing the underlying lung.

Pneumothorax

Pneumothorax is the presence of air in the pleural space that is between the lung and the chest wall. Primary pneumothoraces arise in otherwise healthy people without any lung disease. Secondary pneumothoraces arise in subjects with underlying

lung disease. Despite the absence of underlying pulmonary disease in patients with primary pneumothorax, subpleural blebs and bullae are likely to play a role in the pathogenesis. It is frequently the result of trauma, although sometimes the source of air leak cannot be readily detected.

The radiographic diagnosis of pneumothorax is usually straightforward. A visceral pleural line is seen without distal lung markings. On standard lateral views a visceral pleural line may be seen in the retrosternal position or overlying the vertebrae, parallel to the chest wall [14, 15].

Pneumothoraces present as appearances on lateral chest radiographs; although the value of expiratory views is controversial

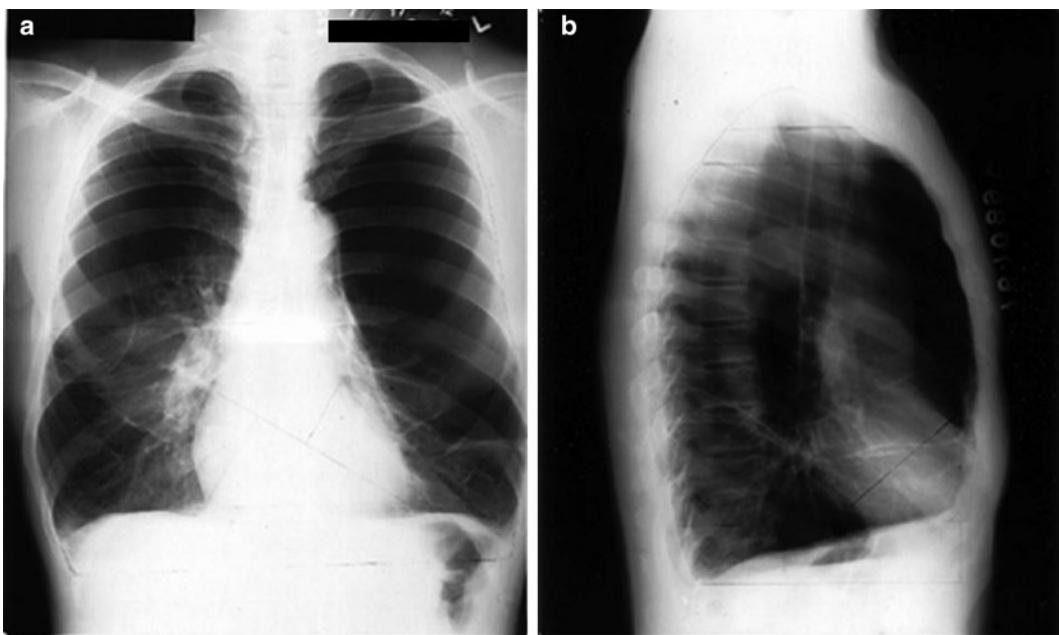


FIG. 3.4. (a) A patient with emphysema. There is a marked hyperinflation with an increase in the anterior–posterior diameter of the chest. Also, there is flattening of the diaphragm bilaterally and a generalized increase in the blackness of the film. (b) The same patient a lateral chest X-ray.

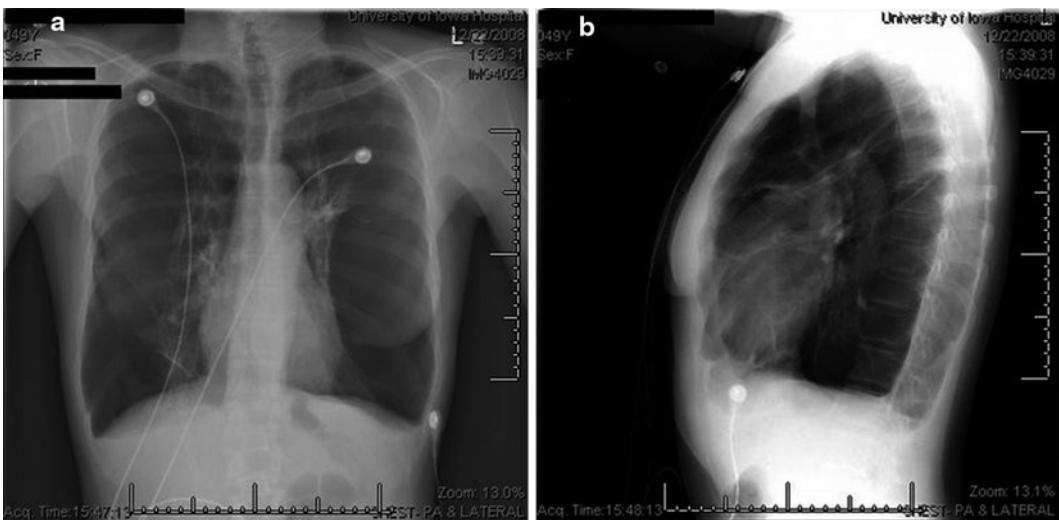


FIG. 3.5. (a) A posterior–anterior chest X-ray of a patient with a bulla in the left hemithorax. (b) The same patient on the lateral radiograph.

many clinicians still find them useful in the detection of small pneumothoraces when clinical suspicion is high and an inspiratory radiograph appears normal. The British Thoracic Society guidelines divide pneumothoraces into small and large based on the distance from visceral pleural surface (lung edge) to chest wall, with less than 2 cm being small and more than 2 cm large [16]. A small rim of air around the lung actually translates into a relatively large loss of lung volume, with a 2-cm deep pneumothorax occupying about 50% of the hemithorax.

In the supine position, air in the pleural space will usually be most readily visible at the lung bases in the cardiophrenic

recess and may enlarge the costophrenic angle. Figure 3.7 shows the chest radiograph of a patient with right-sided pneumothorax.

Several well-known artifactual appearances can mimic the presence of a pneumothorax and should always be remembered during evaluation of chest radiography. The medial border of the scapula can imitate a lung edge but once considered can be traced in continuity with the rest of the bone, revealing its true nature. Skin folds overlying the chest wall can simulate a visceral pleural line and with the relative lack of lung markings in the upper zones, can lead to erroneous



FIG. 3.6. The chest X-ray showing a giant bullae occupying more than two-thirds of the right hemithorax and compressing the underlying lung.

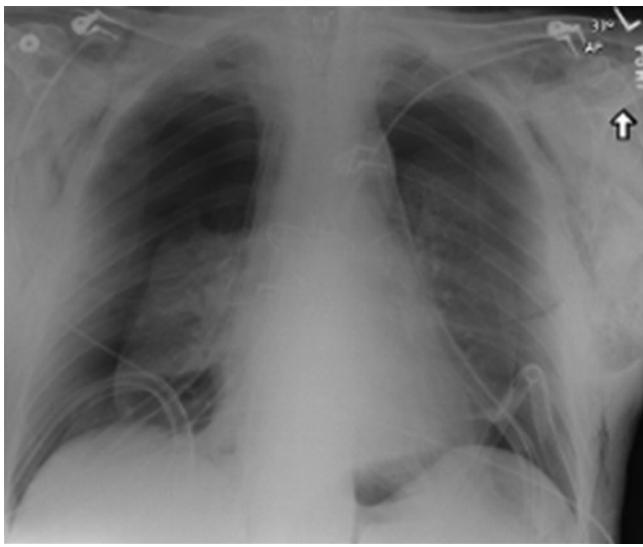


FIG. 3.7. The chest radiograph of a patient with right-sided pneumothorax and bilateral chest tubes.

diagnosis. Once considered, however, the true nature of the image is readily apparent. Skin folds are usually seen to pass outside the chest cavity, are straight or only minimally curved, and do not run parallel to the chest wall as with a true visceral pleural line. Skin folds also form a dense line that is sharp on one side and blurred on the other in contrast to the less dense visceral pleural line. Also, radio-opaque lines are often seen accompanying the inferior margins of ribs, which may simulate a visceral pleural line. These are often called companion shadows although some restrict this term to densities accompanying the first and second ribs. They are caused by protruding extrapleural fat or the subcostal groove.

Tension pneumothorax occurs when the intrapleural pressure exceeds the atmospheric pressure throughout inspiration as well as expiration. It is thought to result from the operation of a one way valve system, drawing air into the pleural space during inspiration and not allowing it out during expiration. The development of tension pneumothorax is often, but not always, heralded by a sudden deterioration in the cardiopulmonary status of the patient related to impaired venous return, reduced cardiac output and hypoxemia. The development of tension in a pneumothorax is not dependent on the size of the pneumothorax and the clinical scenario of tension pneumothorax may correlate poorly with chest radiographic findings [17, 18]. In extreme cases of tension pneumothorax, the air leak brings about significant displacement of the mediastinum and contralateral lung into the opposite hemithorax causing significant hemodynamic instability.

Pleural Effusion

Pleural effusion does not involve the lung parenchyma; it can be the source of a significant amount of absorbing material in the path of the X-ray beam, causing opacity on the films. Large pleural effusions are easy to spot on a chest radiograph but small pleural effusions can be overlooked easily, especially on portable films because the patients are almost always supine or semierect, and the fluid can collect either in a subpulmonic location or deep in the posterior costophrenic sulcus where it is hidden from view. Most often smaller effusions are seen as a veil-like opacity that is most pronounced at the base and tapers towards the lung apex. Figure 3.8 shows a male patient with a large pleural effusion of the left hemithorax occupying two thirds of the chest cavity on the left side.

Chest Tube Placement

In general, appropriate use of chest tubes results in complete drainage of the collected air and fluid in the pleural space and allows full expansion and occupation of the entire pleural space by the lung, thus protecting the lung and pleural space from subsequent complications. Chest tubes are used routinely in the thoracic surgical patient. In practice, there are three main types are used: (a) the large caliber chest tube that involves the use of a 20–30 F size; (b) the small caliber tube, and (c) the pigtail catheters. The typical and most common tubes have a side hole and end hole and, in addition, they have an opaque marker that can be clearly seen in the chest X-radiograph. Many of those chest tubes can be inadvertently placed either in the major fissure, lung parenchyma or too high in the apex, and this can cause severe pain or damage to the lung.

In order to evaluate the position of a chest tube, an anterior-posterior chest radiograph or lateral films are useful [19]. In some circumstances, computed tomography (CT) scans of the chest are valuable for assessing chest tube position; for example, when misplacement is suspected but not confirmed on a plain radiograph [20]. Figure 3.9 shows a chest tube in a female patient placed in the right hemithorax.

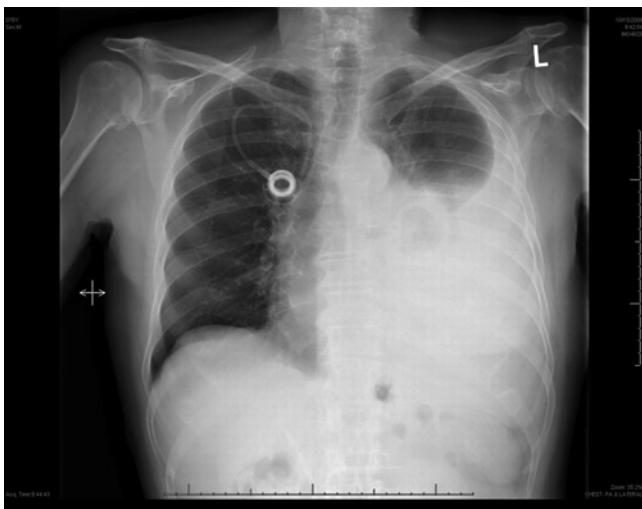


FIG. 3.8. A male patient with a large pleural effusion in the left hemithorax occupying two-thirds of the chest cavity on the left side. Also there is the presence of an infusion port device on the right hemithorax.

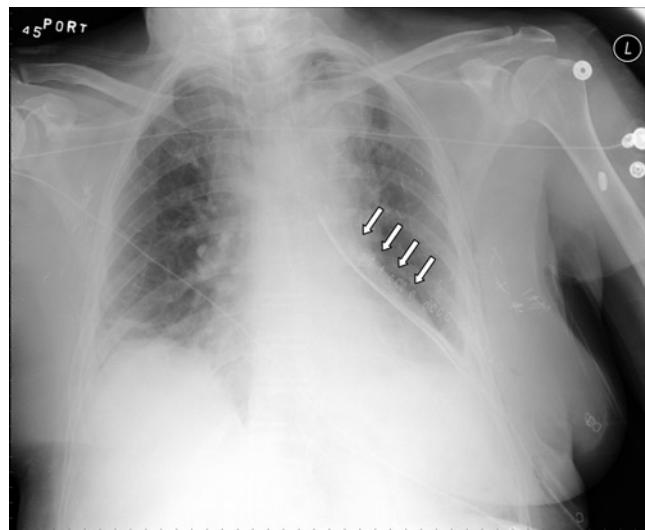


FIG. 3.10. A chest X-ray of a female patient who had a left lower lobe lobectomy. The arrows are pointed to where the stapling line is. Also, there are bilateral infiltrates postlobectomy.



FIG. 3.9. A chest tube in the right hemithorax. The tip of the tube can be clearly seen at the level of the sixth intercostal space. Also, there is a PIC line going from a vein in the right arm to the entrance of the superior vena cava.

Surgical emphysema is a well-known complication of intercostal tube drainage [21]. The development of surgical emphysema associated with pneumothorax involves an air-filled space, not formerly in communication with the subcutaneous tissue, being brought into communication with subcutaneous tissue. This may occur in the presence of a malpositioned, kinked, blocked, or clamped tube. Likewise, a small tube in the presence of a very large leak may potentially

cause surgical emphysema. Any malpositioned chest tube should be visible with the chest radiograph. If the emphysema results in airway obstruction or thoracic compression it may lead to severe respiratory insufficiency. The treatment is usually conservative, but in life-threatening situations, skin incision decompression, and insertions of large bore modified subcutaneous chest drains have all been used successfully.

Previous Lobectomy

Resection of a segment of the lung will produce changes somewhat similar to segmental atelectasis in that a portion of the lung is no longer present, and the remaining segments of the lobe, and other lobes on that side, will expand to fill the space. The chest radiograph will show a displacement of the interlobar fissure and elevation of the diaphragm. There might be a displacement of the hilum. Often the most common sign of the surgery in the chest is the presence of fine metallic sutures on the pleural surface at the site of the resection, and if it is an acute resection (after surgery), the presence of a chest tube. Also, an osteotomy of a rib can be seen in the chest radiograph.

The lobectomy patient will often lead to a greater initial deformity of the involved hemithorax and some shift of the midline structures. As in cases of atelectasis, there should be compensatory overinflation of the noninvolved lobes. Figure 3.10 shows a chest X-ray of a female patient who had a left lower lobe lobectomy.

An important piece of information after lobectomy is the juxtaparenchymal peak sign indicating upper lobe collapse. This is a common finding on chest radiographs of patients after upper lobectomy. It is more frequently seen after right upper lobectomy than after left upper lobectomy and it is more often seen on erect than on supine radiographs. A study has shown that a juxtaparenchymal peak can be expected to appear on chest

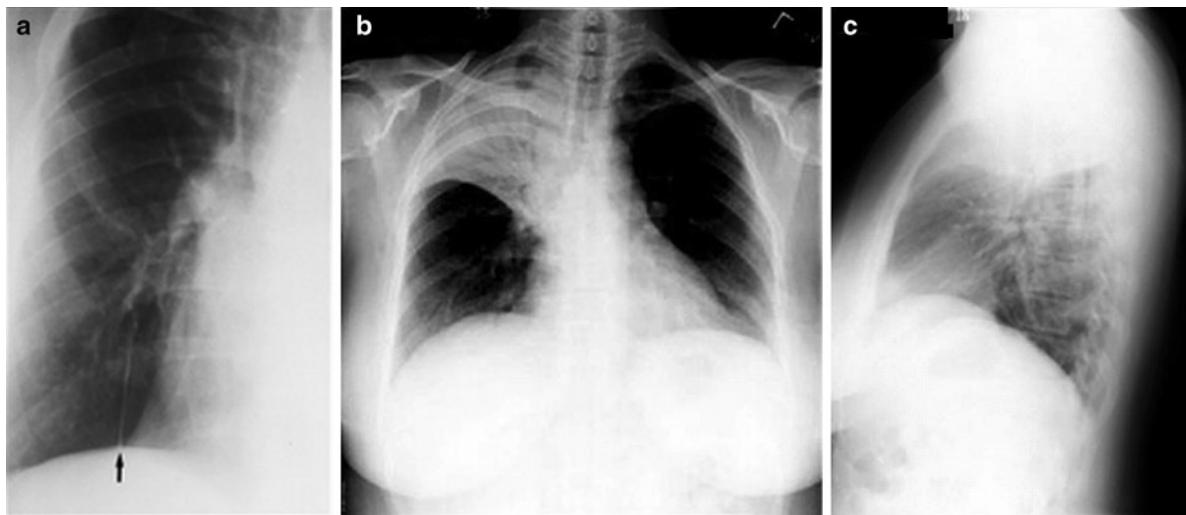


FIG. 3.11. (a) A patient who had a right upper lobectomy showing a thin juxtaparenchymal peak demonstrated by *an arrow*. (b) A right upper lobectomy without the juxtaparenchymal line. (c) Lateral chest radiograph of the same patient.

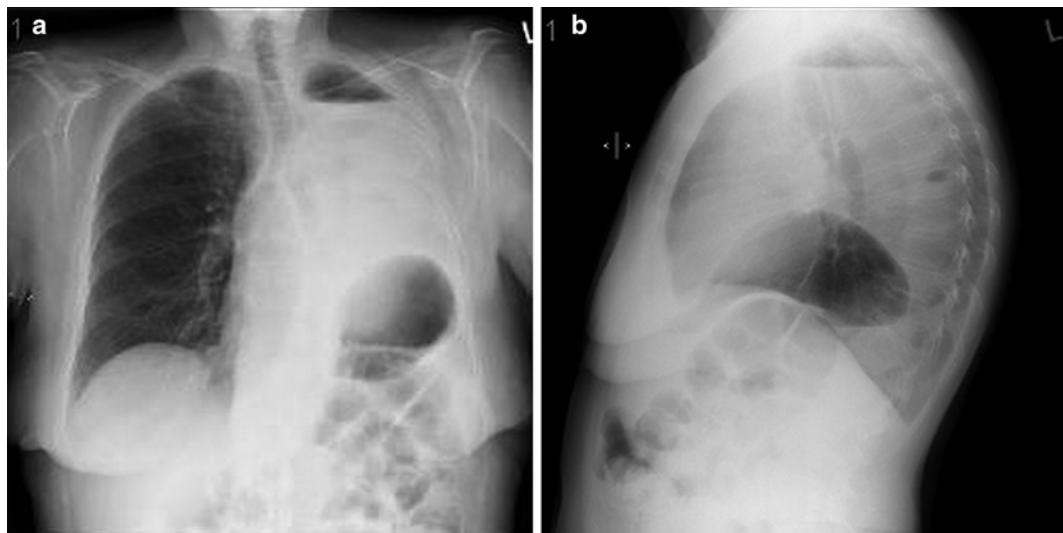


FIG. 3.12. (a, b) A chest radiograph in anterior–posterior and lateral position in a patient after a left-sided pneumonectomy. The opacity in the left lung field is fluid in the hemithorax.

radiographs in about 70% of patients 1 month or more after right upper lobectomy and in 50% after left upper lobectomy [22]. Figure 3.11 shows a patient who had a right upper lobectomy showing a thin juxtaparenchymal peak.

Pneumonectomy

Removal of an entire lung leads to more drastic radiographic changes that evolve with the passage of time. Initially the affected side shows expected postoperative changes at the hilum and chest wall with a complete absence of lung tissue, leaving a very stark, air-filled cavity with extremely sharp margins of the heart and diaphragm. After pneumonectomy, air in the operated hemithorax is gradually reabsorbed and replaced by fluid with a net volume loss. As a result, the

trachea and mediastinum gradually shift towards the surgical side. In the immediate postoperative period, a mediastinal shift away from the surgical side indicates atelectasis of the contralateral lung or an abnormal accumulation of air or fluid on the surgical side [23]. A rapid mediastinal shift can signify the presence of an air leak with a “ball-valve” effect leading to a tension pneumothorax. There is usually some elevation of the hemidiaphragm and a shift of the heart and other midline structures towards the operated side as the remaining lung expands to take some of the space. Gradually the hemithorax fills with fluid, showing a distinct air fluid level if the patient is upright or a more subtle increase in opacity if the patient is in the supine position. Figure 3.12 shows a chest radiograph in anterior, posterior, and lateral position in a patient with a left-sided pneumonectomy.

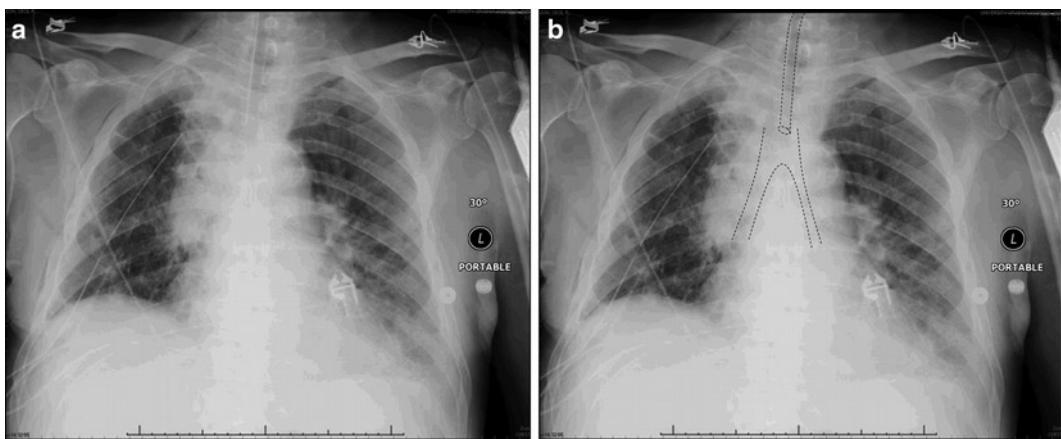


FIG. 3.13. (a) A male patient that underwent a right upper lobectomy and remained intubated in the postoperative period with a single-lumen endotracheal tube. (b) The same patient with a reconstruction of the single-lumen endotracheal tube. Notice that the tip of the single-lumen endotracheal tube should be placed 3 cm above the tracheal carina.

Single-Lumen Endotracheal Tubes

After a thoracic surgical procedure, a chest radiograph film is required in order to assess lung expansion, chest tube placement, and if the patient remains intubated the proper placement of the endotracheal tube must be assessed. The proper position of a single-lumen endotracheal tube as seen in the chest radiograph is that the distal tip of the tube is located approximately 3 cm above the tracheal carina. All endotracheal tubes have opaque markers that can be clearly identified in the radiographs. Figure 3.13a shows a male patient that underwent a right upper lobectomy and remained intubated in the postoperative period with a single-lumen endotracheal tube. Figure 3.13b shows the same patient with a reconstruction of the single-lumen endotracheal tube.

Double-Lumen Endotracheal Tubes

With any thoracic surgical procedure involving lung isolation devices, the anesthesiologist must review the tracheobronchial anatomy in the preoperative visit to determine whether or not abnormal anatomy exists. A view of the posteroanterior chest radiograph will allow assessment of the shadow of the tracheobronchial anatomy along with the bronchial bifurcation. It is estimated that in 75% of the films, the left mainstem bronchus shadow is seen. In addition, the chest radiograph can be useful to determine the proper size of a left-sided DLT. Brodsky et al. [24] reported that measurement of the tracheal diameter at the level of the clavicle on the preoperative posteroanterior chest radiograph can be used to determine proper left-sided DLT size (refer to Chap. 16). Figure 3.14 shows the measurement of the tracheal width at the level of the clavicles to estimate the proper size of the left-sided DLT from a chest radiograph. The tip of each lumen is identified with a radiopaque marker. Figure 3.15a shows the chest



FIG. 3.14. The measurement of the tracheal width at the level of the clavicles to estimate the proper size of the left-sided DLT from a chest radiograph. The arrow points to the clavicle.

radiograph of a patient with a left-sided DLT in place. Notice the endobronchial lumen is approximately 2 cm below the tracheal carina into the left mainstem bronchus. Figure 3.15b shows a reconstruction of the DLT which is marked in the chest radiograph.

Postoperative Acute Lung Injury

Acute lung injury (ALI) may complicate thoracic surgery and is a major contributor to postoperative mortality. The incidence of ALI after thoracic surgery is estimated to be 4.2% [25, 26]. In a study by Licker et al. [25], they found a biphasic distribution pattern of ALI after lung resection. The primary

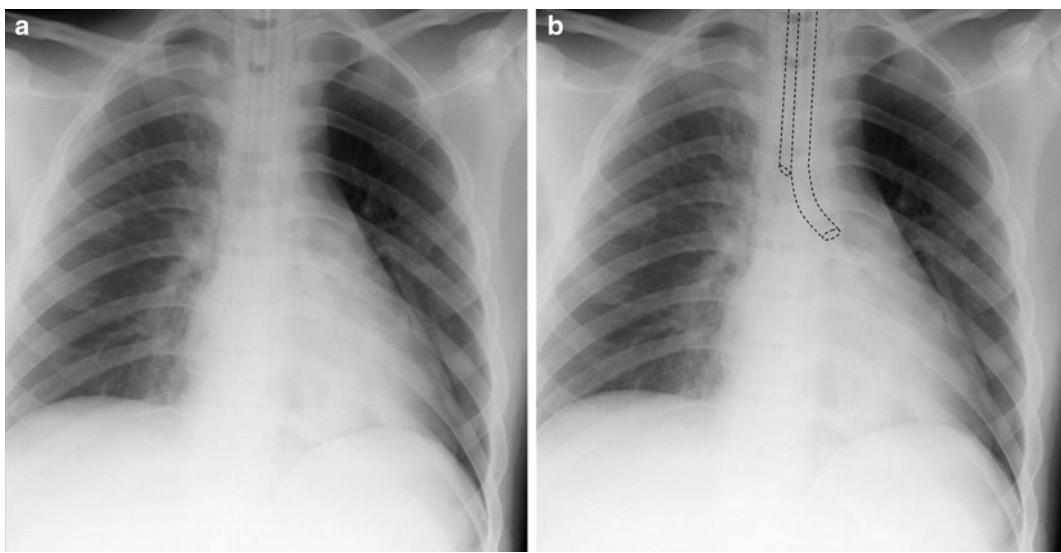


FIG. 3.15. (a) The chest radiograph of a patient with a left-sided DLT in place. Notice the endobronchial lumen is approximately 2 cm below the tracheal carina into the left mainstem bronchus. (b) A reconstruction of the DLT which is marked in the chest radiograph.

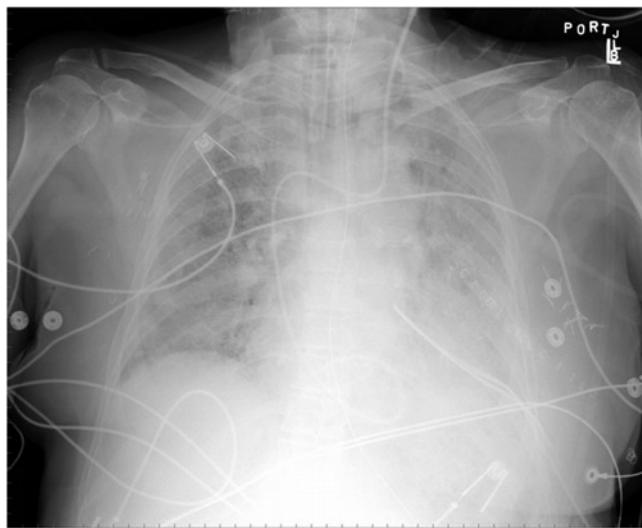


FIG. 3.16. A patient with an acute lung injury (ALI) 72 h postoperatively, the interstitial edema has progressed in the chest X-radiograph. There is a single-lumen endotracheal tube in place; also a pulmonary artery catheter introduced via the left internal jugular vein is seen. The chest radiograph also shows bilateral diffuse fluffy opacities typical of interstitial pulmonary edema postlobectomy.

form developed within the first 3 days after surgery and a secondary form triggered the onset of ALI after the third postoperative day.

The clinical presentation is a severe respiratory insufficiency with a progressive hypoxemia that does not respond to a conventional treatment including O_2 therapy. The chest radiograph of a patient with an ALI appears as patchy, unilateral or bilateral infiltrates, dependent pulmonary edema. In addition, atelectatic zones can be seen in the chest radiograph.

Figure 3.16 shows a 60-year-old female following a left lower lobectomy that developed ALI in the immediate postoperative period, on the chest radiograph taken after 72 h the interstitial edema has progressed. There is a single-lumen endotracheal tube in place; also a pulmonary artery catheter introduced via the left internal jugular vein can be seen. The chest radiograph also shows bilateral diffuse fluffy opacities typical of interstitial pulmonary edema postlobectomy after ALI.

Computed Tomography Scan and Pulmonary Disease

CT scan of the chest is used as a diagnostic study; this is usually done after abnormal findings on a standard chest radiograph [27]. Common indications of CT includes: staging of lung cancer, solitary pulmonary nodule, mass or opacity, diffuse infiltrative lung disease, widened mediastinum, mediastinal mass, or other abnormalities of the mediastinum pleural abnormalities, chest wall lesions, trauma, etc. Also, CT provides valuable information for the clinician with regard to the airway compression at any level of the tracheobronchial tree, as well as vascular compression diagnosis [28–31].

CT scans are performed in deep inspiration and at total lung capacity. For a routine helical CT of the chest, 2.5–5 mm sections are usually recommended. Thinner (1–2.5 mm) sections can be used to study fine details of the lung parenchyma. On routine studies, the field of view is adjusted to the size of the thorax, but small fields of view may be selected for smaller anatomic parts that require study. In addition, a contrast CT scan is useful in suspected vascular abnormalities such as pulmonary embolism. Recent improvements in scanner technology have led to the introduction of spiral or helical volumetric CT.

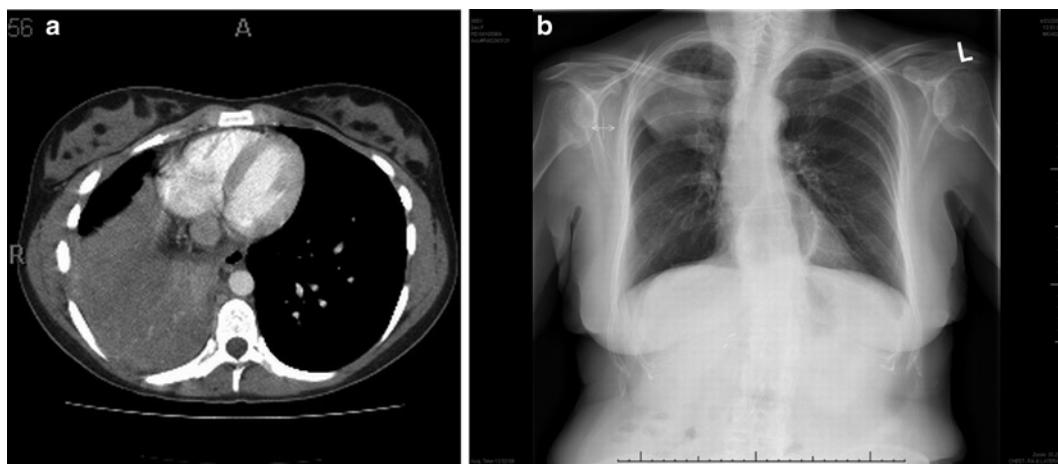
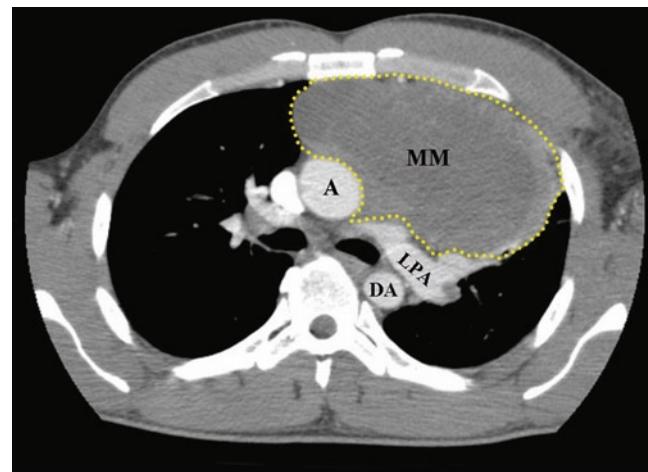


FIG. 3.17. (a) A computed tomography (CT) scan of the chest. Diagnosis of tumor of the lung. (b) The chest radiograph showing the lung mass in the right upper lobe in the same patient. Diagnosis of right upper lobe adenocarcinoma.

Computed Tomography Scan and Lung Mass, Mediastinal Mass, Pleural Effusion, and Pericardial Effusion

CT scan of the chest will confirm the presence of a mass in the chest and in many instances the specific location. Figure 3.17a shows a CT scan of the chest. There is the presence of a lung mass on the right lung. Figure 3.17b shows the chest radiograph showing the lung mass in the right upper lobe in a female patient. In addition, the CT scan of the chest will define the precise size and location of the mediastinal mass, any involvement with adjacent structures as well as the degree of compression of the airway (trachea and/or bronchi). It is important during the assessment of the CT scan to identify the location of the mass, define its relationship to adjacent structures, assess the extent and degree of tracheal and/or vascular compression, and assess the patency of the airway at the tracheal and bronchial level. The CT scan also will permit accurate measurement of the airway diameter and will determine the precise level and extent of compression of the trachea. As mentioned previously, the average cross-sectional diameter of the trachea in a 70-kg, 170-cm tall person is approximately 18–23 mm. A tracheal diameter narrowing of 10 mm on CT corresponds to a 50% reduction in the tracheal cross-sectional area at that level. Figure 3.18 shows a CT scan of the chest with a large anterior mediastinal mass in the left hemithorax. Figure 3.19 shows a CT scan of the chest with a large anterior mediastinal mass on the left side causing compression to the entrance of the left mainstem bronchus.

A CT scan of the chest allows precise location of the extra-pulmonary fluid whether in the peripheral pleural space or the interlobar fissure. Figure 3.20 shows a CT scan of the chest showing a large pleural effusion on the left hemithorax. Also, the CT scan is very useful for the diagnosis of pericardial effusions, because the precise location can be identified with this

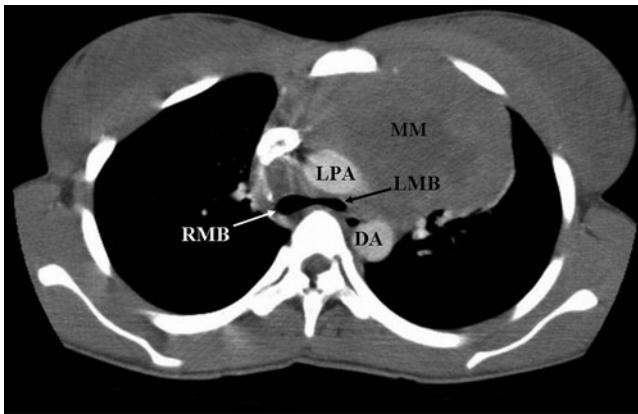


A = aorta
DA = descending aorta
LPA = left pulmonary artery
MM = mediastinal mass

FIG. 3.18. A computed tomography scan of the chest with a large anterior mediastinal mass in the left hemithorax (the dotted line is surrounding the mass). This patient has a diagnosis of mediastinal mass, diffuse B-cell lymphoma.

method. Figure 3.21 shows a pericardial effusion; notice the fluid in the pericardial sac.

In addition, a different alternative to assess the airways while using a CT scan is with the three-dimensional (3D) reconstruction of the airway using a workstation connected to a multidetector CT (MDCT) scanner. The MDCT provides high spatial resolution images of the whole lung without any anatomical gap. The technique consists of projecting the voxels with the lowest alteration value in every view through the volume explored, at various angles depending on the airway involved. If a tracheobronchial injury is suspected, 3D extraction of the



LMB = left mainstem bronchus
RMB = right mainstem bronchus

FIG. 3.19. A computed tomography scan of the chest with a large anterior mediastinal mass on the left side causing compression to the entrance of the left mainstem bronchus. Diagnosis in this patient is germ cell tumor.



FIG. 3.20. A CT scan of the chest showing a large pleural effusion in the left hemithorax. Also, the CT scan is very useful for the diagnosis of pericardial effusion.

airways may be useful by focusing the 3D volume-rendering technique to the tracheobronchial tree [32]. This technique is used for analyzing stenosis or distortion of the tracheobronchial tree but also may allow the diagnosis of tracheobronchial injury by demonstrating a wall defect and or abnormal position of lobar and segmental bronchi [33, 34].

Also, a 3D scan of the chest is another modality to identify lymph nodes. The development of virtual bronchoscopy has led interest in introducing CT based computer-graphic techniques into the procedure of lung cancer staging. In virtual bronchoscopy, the 3D CT image serves as a high-resolution digital image replica of the chest [35]. Endoluminal renderings of the airways



FIG. 3.21. A pericardial effusion; notice the fluid in the pericardial sac.

can be generated along paths following the airway central axes and lead to an off-line simulation of videobronchoscopy as virtual endoscopy, interior views are computer-generated from radiologic images (see also Chap. 16, Fig. 16.14).

Multidetector Computer Tomography Scan of the Chest

Modern MDCT scanners readily provide very large high-resolution 3D volumetric images of the chest. Many 3D visualization techniques have been devised for more exhaustively viewing of the information contained in 3D MDCT chest images. The 3D MDCT image provides views of the segments of the airway tree, computes the central axes of the extracted airways, and also defines the endoluminal and exterior surfaces of the segmented airway tree and the exterior surfaces of the regions of interest for rendering [36].

One of the advantages of the MDCT and 3D reconstruction of the tracheobronchial tree is that it allows us to appreciate distorted tracheobronchial anatomy or changes in the airway with age. Figure 3.22 shows a MDCT scan of the chest on a male patient.

Magnetic Resonance Imaging and Pulmonary Disease

MRI produces images that superficially appear similar to CT scans. The MRI provides greater contrast resolution than CT scans and offers the potential for tissue characterization [37]. Also MRI of pulmonary parenchymal disease using a modified breath-hold 3D gradient echo technique allows imaging of a wide spectrum of solid and nonsolid pulmonary parenchymal diseases with reproducible high image quality, effective suppression of artifacts, high resolution and visualization [38].

The 3D gradient echo technique allows better visualization of peripheral and central parenchyma, pulmonary arteries, heart and esophagus.

The MRI images are computer-generated images, usually in cross-sectional orientation but also with direct sagittal or coronal views, with tissues displayed in varying shades of black, white, and gray. MRI scans rely primarily on the evaluation of the amount of protons (water) in different tissues. This data information is acquired by placing the patient in a powerful



FIG. 3.22. A multidetector computed tomography scan of the chest of a male patient.

magnetic field and interrogating the body with radio waves of a specific frequency; then listening for the response. By varying the frequency of the radio wave, the body can be imaged in multiple planes, not just in axial sections. Direct sagittal and coronal images enable the radiologist to evaluate involvement of lung prosenchyma [39], mediastinal structure, and the chest wall with greater clarity than with a CT scan. In addition, MRI is an adjunct to CT scan evaluation reserved for patients in whom CT scans did not resolve the anatomic issues or for whom additional information about the mediastinal and its relationship to other vital organs are required including invasion to heart or great vessels [30, 40, 41]. Figure 3.23 shows MRI of the chest in a patient with a mediastinal mass.

Summary

Radiological studies play an important role in the diagnosis and treatment of the thoracic surgical patient in the preoperative, intra- and postoperative period. Chest radiographs allow us to identify distorted tracheobronchial anatomy, presence of lung masses, lung collapse, chest tube placement, endotracheal tube placement, and lung expansion or shifting of mediastinum in cases of tension pneumothorax. CT scans of the chest permit an identification and precise location of lung masses, mediastinal masses, or the presence of fluid and compromise to adjacent structures.

Multidetector computed tomography scan and 3D reconstruction allows identification of tracheobronchial anatomy in a more precise form. All radiological studies must be reviewed in the preoperative evaluation of thoracic surgical patients. In cases where the diagnosis or anatomy is unclear, these studies must be reviewed in conjunction with a thoracic surgeon or a radiologist.

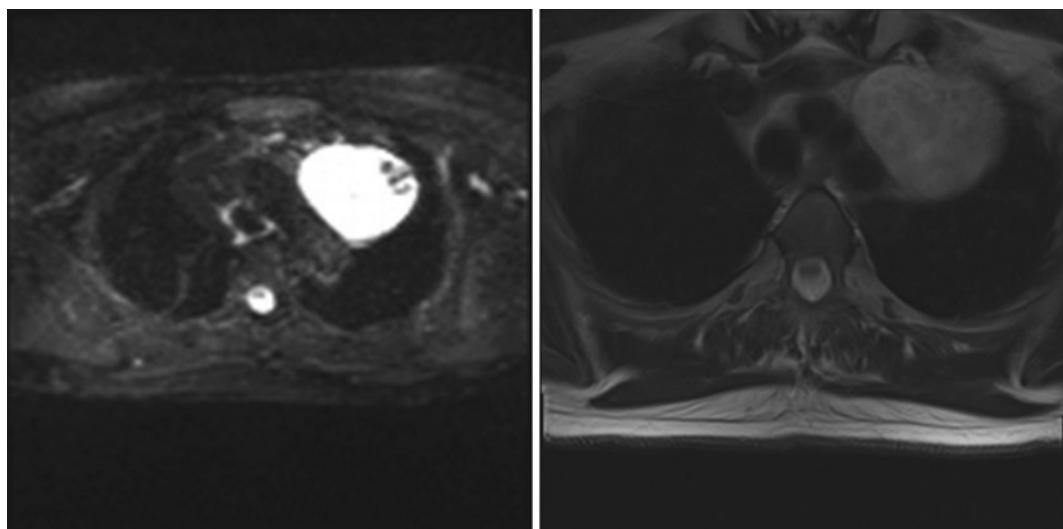


FIG. 3.23. A magnetic resonance imaging (MRI) of the chest. This patient has a diagnosis of Schwannoma.

References

- Boiselle PM. Imaging of the large airways. *Clin Chest Med.* 2008;29:181–93.
- Seymour AH. The relationship between the diameters of the adult cricoid ring and main tracheobronchial tree: a cadaver study to investigate the basis for double-lumen tube selection. *J Cardiothorac Vasc Anesth.* 2003;17:299–301.
- Minnich DJ, Mathisen DJ. Anatomy of the trachea, carina and bronchi. *Thorac Surg Clin.* 2007;17:571–85.
- Stene R, Rose M, Weigner MB, et al. Bronchial trifurcation at the carina complicating use of a double-lumen tracheal tube. *Anesthesiology.* 1994;80:162–1164.
- Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic anesthesia. *Curr Opin Anaesthesiol.* 2009;22:4–10.
- Goldwin RL, Reed JC. Radiology of the chest. Chapter 2. In: Kaplan J, Slinger P, editors. *Thoracic anesthesia.* 3rd ed. New York: Churchill Livingstone; 2003. p. 24–56.
- Fraser RS, Pare' JA, Fraser RG, et al. *Synopsis of diseases of the chest.* 2nd ed. Philadelphia: WB Saunders; 1994.
- Datt V, Tempe DK. Airway management in patients with mediastinal masses. *Indian J Anaesth.* 2005;49:344–52.
- Ahmed-Nusrath A, Swanevelder J. Anesthesia for mediastinoscopy. *Contin Educ Anaesth Crit Care Pain.* 2007;7:6–9.
- Campos JH. Managing the patient with an anterior mediastinal mass. Chapter 11. In: Cohen NH, editor. *Medically challenging patients undergoing cardiothoracic surgery.* Society of Cardiovascular Anesthesiologists Monograph. Baltimore: Lippincott Williams & Wilkins; 2009. p. 285–302.
- Harris GJ, Harman PK, Trinkle JK, et al. Standard biplane roentgenography is highly sensitive in documenting mediastinal masses. *Ann Thorac Surg.* 1987;44:238–41.
- Morgan MDL, Edward CW, Morris J, et al. Origin and behavior of emphysematous bullae. *Thorax.* 1989;44:533–8.
- Schipper PH, Meyers BF, Battafarano RJ, et al. Outcomes after resection of giant emphysematous bullae. *Ann Thorac Surg.* 2004;78:976–82.
- O'Connor AR, Morgan WE. Radiological review of pneumothorax. *BMJ.* 2005;330:1493–7.
- Glazer H, Anderson DJ, Wilson BS, et al. Pneumothorax: appearances on lateral chest radiographs. *Radiology.* 1989;173:707–11.
- Henry M, Arnold T, Harvey J. BTS guidelines for the management of spontaneous pneumothorax. *Thorax.* 2003;58 Suppl 2:ii39–52.
- Light RW. Tension pneumothorax. *Intensive Care Med.* 1994;20:468–9.
- Baumann MH, Sahn SA. Tension pneumothorax: diagnostic and therapeutic pitfalls. *Crit Care Med.* 1994;22:896.
- Symbas PN. Chest drainage tubes. *Surg Clin North Am.* 1989;69:41–6.
- Baldt MM, Bankier AA, Germann PS, et al. Complications after emergency tube thoracostomy: assessment with CT. *Radiology.* 1995;195:539–43.
- Maunder RJ, Pierson DJ, Hudson LD. Subcutaneous and mediastinal emphysema. Pathophysiology, diagnosis, and management. *Arch Intern Med.* 1984;144:1447–53.
- Konen E, Rozenman J, Simansky DA, et al. Prevalence of the juxtaphrenic peak after upper lobectomy. *Am J Roentgenol.* 2001;177:869–73.
- Wechsler RJ, Goodman LR. Mediastinal position and air-fluid height after pneumonectomy: the effect of the respiratory cycle. *Am J Roentgenol.* 1985;145:1173–6.
- Brodsky JB, Macario A, Mark JB. Tracheal diameter predicts double-lumen tube size: a method for selecting left double-lumen tubes. *Anesth Analg.* 1996;82:861–4.
- Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97:1558–65.
- Hayes JP, Williams EA, Goldstraw P, et al. Lung injury in patients following thoracotomy. *Thorax.* 1995;50:990–1.
- McLoud T. Imaging the lungs. Chapter 36. In: Patterson, Cooper, Deslauriers, Lerut, Luketich, Rice, editors. *Pearson's thoracic surgery.* 3rd ed. New York: Churchill Livingstone; 2008. p. 415–28.
- Harte BH, Jaklitsch MT, McKenna SS, et al. Use of a modified single-lumen endobronchial tube in severe tracheobronchial compression. *Anesthesiology.* 2002;96:510–1.
- Slinger P, Karsli C. Management of the patient with a large anterior mediastinal mass: recurring myths. *Curr Opin Anaesthesiol.* 2007;20:1–3.
- Chiles C, Woodard PK, Gutierrez FR, et al. Metastatic involvement of the heart and pericardium: CT and MR imaging. *Radiographics.* 2001;21:439–49.
- Shepard JA, Grillo HC, McLoud TC, et al. Right-pneumonectomy syndrome: radiologic findings and CT correlation. *Radiology.* 1986;161:661–4.
- Le Guen M, Beigelman C, Bouhemad B, et al. Chest computed tomography with multiplanar reformatted images for diagnosing traumatic bronchial rupture: a case report. *Crit Care.* 2007;11:1–8.
- Rubin GD, Beaulieu CF, Argiro V, et al. Perspective volume rendering of CT and MR images: applications for endoscopic imaging. *Radiology.* 1996;199:321–30.
- Boiselle PM, Reynolds KF, Ernst A. Multiplanar and three-dimensional imaging of the central airways with multidetector CT. *Am J Roentgenol.* 2002;179:301–8.
- Higgins WE, Ramaswamy K, Swift RD, et al. Virtual bronchoscopy for three-dimensional pulmonary image assessment: state of the art and future needs. *Radiographics.* 1998;18:761–78.
- Higgins WE, Helferty JP, Lu K, et al. 3D CT-video fusion for image-guided bronchoscopy. *Comput Med Imaging Graph.* 2008;32:159–73.
- Moore EH, Webb WR, Muller N, et al. MRI of pulmonary air-space disease: experimental model and preliminary clinical results. *Am J Roentgenol.* 1986;146:1123–8.
- Bader TR, Semelka RC, Pedro MS, et al. Magnetic resonance imaging of pulmonary parenchymal disease using a modified breath-hold 3D gradient-echo technique: initial observations. *J Magn Reson Imaging.* 2002;15:31–8.
- Bergin CJ, Glover GH, Pauly JM. Lung parenchyma: magnetic susceptibility in MR imaging. *Radiology.* 1991;180:845–8.
- Bremerich J, Roberts TP, Wendland MF, et al. Three-dimensional MR imaging of pulmonary vessels and parenchyma with NC100150 injection (Clariscan). *J Magn Reson Imaging.* 2000;11:622–8.
- Bittner RC, Felix R. Magnetic resonance (RM) imaging of the chest: state-of-the-art. *Eur Respir J.* 1998;11:1392–404.

4

Essential Anatomy and Physiology of the Respiratory System and the Pulmonary Circulation

J. Michael Jaeger and Randal S. Blank

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Key Points

- Knowledge of the clinical anatomy and function of the respiratory system is essential for the safe, efficient, and appropriate perioperative management of intubation, mechanical ventilation, and anesthesia for the thoracic surgical patient.
- The lung has ten (third generation airway) bronchopulmonary segments on the right and eight segments on the left that are readily identifiable by fiberoptic bronchoscopy (two segmental bronchi on the left are considered “fused”).
- The anesthetic employed, both general and regional, will impact the control of respiration, reactivity of the airways, and the patient’s ability to maintain their airway, take a deep breath, and cough.
- Dynamic influences of ventilatory pattern, posture, body habitus, agitation or pain, and inflammation can cause “air trapping” and drastically reduce alveolar ventilation.
- The compliance and resistance of the respiratory system will change during the course of surgery, especially

those procedures requiring one-lung ventilation, and may necessitate frequent adjustments of the ventilator to optimize gas exchange and reduce lung injury.

- Many drugs employed during cardiothoracic surgery will impact the lung’s intrinsic mechanisms to match ventilation to perfusion matching either directly on hypoxic pulmonary vasoconstriction (HPV) or indirectly by altering cardiac output or vascular resistance.

Introduction

Appropriate perioperative management of the thoracic surgical patient requires an appreciation of the uniqueness and complexity of the anatomy and function of the respiratory system. It is particularly suited to perform a wealth of tasks including gas exchange between the lungs and blood, speech, protection from airborne environmental insults and pathogens, and a host of metabolic functions (repair, growth). While some of these functions have little importance for the anesthesiologist during

the course of a surgical procedure, optimizing gas exchange, controlling pulmonary arterial pressure, and maintaining blood flow require constant attention. Furthermore, the dynamic interaction between the cardiovascular system and the respiratory system can be altered by changes in position, medications and anesthetics, mechanical ventilation, surgical interventions, disease processes, etc. The impact of these alterations cannot be underestimated. The entire cardiac output passes from the right side of the heart to the left side with each heartbeat; therefore what affects the pulmonary circulation ultimately impacts the systemic circulation. While an in-depth discussion of the physiology and anatomy of the entire respiratory system is beyond the scope of this chapter, the essentials will be discussed with the goal of providing insights into the clinical relevance and application of this knowledge by the thoracic anesthesiologist.

Functional Anatomy

Upper Airway Anatomy

Oropharynx and Nasopharynx

The collection of air passages extending from the nares and lips through the labyrinthine nasopharynx and oropharynx extending through the larynx to the cricoid cartilage can be defined as the functional upper airway. This airway complex serves a host of functions: warming and humidifying the passage of air, filtering particulate matter, and preventing aspiration during deglutition.

In normal quiet breathing, air enters the nose, a complex chamber separated medially its entire length by a cartilaginous and bony septum (vomer). It is bounded laterally by the inferior, middle, and superior turbinates overlying the sinus ostia and inferiorly by the hard and soft palates before emptying into the nasopharynx. The mucosa covering these structures is highly vascular and innervated which must be appreciated when performing nasopharyngeal intubation with endotracheal tubes, nasogastric sumps or feeding tubes, or fiberoptic bronchoscopes. Furthermore the nasal passages represent a significant resistance to airflow, normally double than that found in mouth breathing. Airflow resistance increases dramatically when nasal polyps are present, the mucosa is inflamed and edematous, or when high air flows must be achieved as in heavy exercise.

The pharynx is 12–15 cm long and is divided into the nasopharynx (from the soft palate to the tip of the uvula), the oropharynx (from the anterior pillars of the tonsillar fossa to the epiglottis) that includes the pharyngeal portion of the genioglossus muscle, and finally the laryngopharynx lying posterior to the larynx. Supination, sleep, and general anesthesia may promote obstruction of the oropharynx by the tongue, hard palate, and pharyngeal musculature as their tone decreases [1, 2]. Hyperextension or hyperflexion of the cervical spine generally increases upper airway resistance [3].

During inspiration, a nonsedated, spontaneously breathing patient dilates the oropharyngeal pharynx by contracting the genioglossus muscle and elevating the tongue off the pharyngeal wall in a coordinated reflex possibly involving thoracic muscle activity [2, 3].

Larynx

The larynx is a complex structure overlying the fourth to the sixth cervical vertebra and consists of several muscles, their ligaments and cartilaginous anchors, and significant innervation (Fig. 4.1). The inlet of the larynx is defined by the epiglottis, aryepiglottic folds, and the arytenoids. The larynx itself bulges into the pharynx posteriorly creating a deep pharyngeal recess anterolaterally on either side, the pyriform fossa. The bilateral pyriform fossae or recesses are clinically relevant because of their tendency to trap food or foreign objects (and tubes or probes) in the pharynx and as potential sites for the application of topical anesthesia to block the internal branch of the superior laryngeal nerve. The larynx serves as the organ of phonation, plays an important role in coughing, and in protection of the airway during deglutition [4].

The primary structure of the larynx is the thyroid cartilage that forms the point of articulation of the paired arytenoid cartilages with the vocal ligaments and their controlling musculature. However, other essential structures include the hyoid bone and its attachments, the epiglottis, the cricoid cartilage, and the corniculate cartilages. The hyoid bone is a U-shaped bone that is attached to the mandible and tongue by the hyoglossus, the mylohyoid, geniohyoid, and digastric muscles, to the stylohyoid

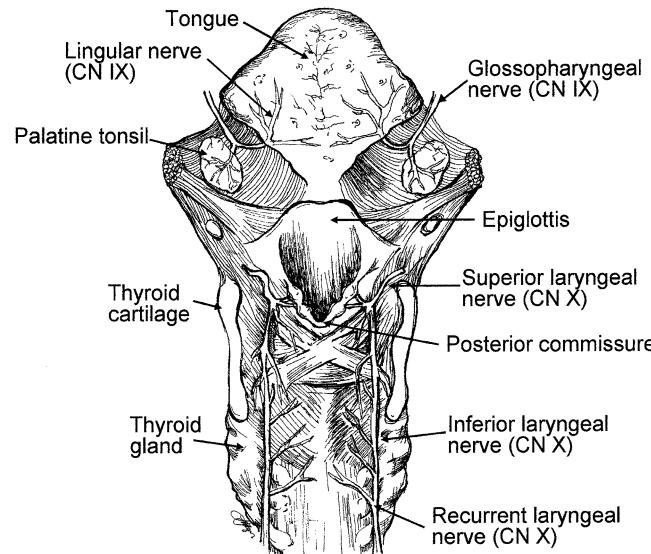


FIG. 4.1. Diagram of the larynx from the base of the tongue to below the thyroid cartilage as viewed from its posterior aspect. Note the relationship of the superior laryngeal, inferior laryngeal, and recurrent laryngeal nerves and the posterior aspect of the larynx, thyroid, and trachea. Tracheal and thyroid surgery places these nerves at risk.

ligament and muscle, and to the pharynx by the middle pharyngeal constrictor muscle. Beneath the hyoid bone is slung the remainder of the larynx by its attachment, the thyrohyoid membrane and muscle. While its function other than as a flexible anchor is unclear, it is possible to bisect its mandibular attachments (“suprathyroid release”) and mobilize the larynx in order to facilitate its caudal displacement in tracheal resection procedures. The epiglottis is the midline “leaf-shaped” elastic cartilage found inferior to the base of the tongue. It is anchored anteriorly to the hyoid bone and inferiorly to the inside of the anterior portion of the thyroid cartilage immediately above the vocal cords. Bilateral folds of the epiglottis curve posteriorly to form a mucosal ridge attaching to the arytenoid cartilages sitting on top of the posterior lamina of the cricoid, the aryepiglottic folds. The epiglottis, aryepiglottic folds, and the corniculate tubercles form the readily recognizable inlet into the glottis below. The large thyroid cartilage defines the larynx with its paired lamina fused anteriorly at the laryngeal prominence and extending posteriorly to terminate in superior and inferior horns or cornu. The thyroid cartilage serves as a stable point of attachment for numerous small muscles and ligaments which manipulate the small arytenoids, corniculates, and vocal cords. The thyroid cartilage also attaches to the cricoid ring in ways which afford it some degree of mobility. One key ligament deserves special attention, the vocal ligament or true vocal cord. The paired vocal cords attach posteriorly to the vocal process of each arytenoid and stretch anteriorly to meet at the junction of the thyroepiglottic ligament of the anterior thyroid cartilage. The triangular opening formed by the vocal ligaments is the glottis with its apex anterior (Fig. 4.2). The mean length of the relaxed open glottis is approximately 23 mm in males and 17 mm in females. The glottis at its widest

(posterior) point is 6–9 mm but can be “stretched” to 12 mm [5]. It should be noted that the vocal cords are covered by only a thin, adherent mucosa, producing the pearly white appearance. The absence of any submucosa implies that the vocal cords are unlikely to “swell” significantly as there is minimal space to accumulate edema fluid. The folds of mucosa and fibrous tissue lying parallel to the true vocal cords just superiorly in the glottis, the vestibular folds or “false vocal cords,” can become edematous. The intrinsic laryngeal musculature function is to open the glottis in inspiration, close the glottis, and constrict the superior structures in deglutition, and finely control abduction, adduction, and tension of the true vocal cords in phonation.

Pharyngeal Innervation

Innervation of the pharynx is distributed among several sensory and motor branches of the glossopharyngeal and vagus (external and internal branches of the superior laryngeal nerves, recurrent laryngeal nerves). The nasopharynx sensory innervation is derived from the maxillary division of the trigeminal nerve, while the oropharynx is diffusely innervated by sensory branches from the glossopharyngeal nerve. The internal branch of the superior laryngeal nerve pierces the lateral aspect of the thyrohyoid membrane along with the superior laryngeal artery and vein to provide sensation for the base of the tongue, vallecula, epiglottis, aryepiglottic folds, pyriform recesses, and the superior aspect of the true vocal cords. The external branch of the superior laryngeal nerve provides motor to the cricothyroid muscle, a tensor of the true vocal cords. The recurrent laryngeal nerves supply sensation to the vocal cords and tracheobronchial tree as well as motor to the remaining intrinsic musculature of the larynx. The right recurrent laryngeal nerve originates at the level of the right subclavian artery but the left originates at the level of the aortic arch and loops around the ligamentum arteriosum before both ascend cephalad along the tracheoesophageal groove. This fact that must be appreciated during esophageal surgery and during both cervical and anterior mediastinoscopy, as these structures can be at risk. The larynx receives its blood supply from the superior and inferior laryngeal arterial branches of the superior and inferior thyroid arteries, respectively. These arteries follow the course of the superior and recurrent laryngeal nerves.

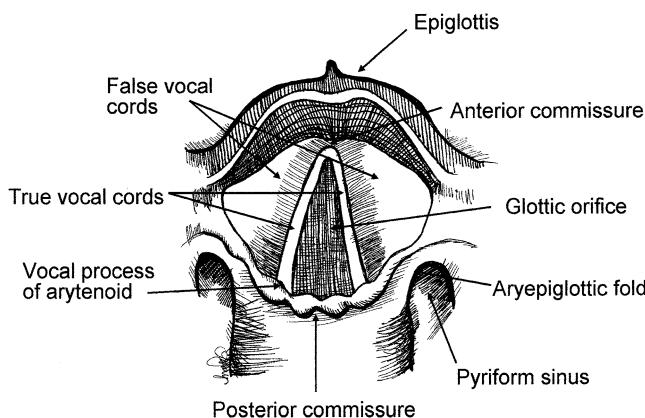


FIG. 4.2. Diagram of the glottis as seen from above using a laryngoscope or fiberoptic bronchoscope. Note the triangular shaped glottic introitus with its narrowest aspect at the anterior commissure. Passage of bronchoscopes, endotracheal tubes, and especially double-lumen tubes should be directed posteriorly where the vocal cords will spread the widest. Note that the vocal process of the arytenoid cartilage pivots on a small point and can be traumatized and displaced with rough handling.

Upper Airway Function

Homeostatic Mechanisms

The most obvious function of the upper airways is to provide a durable protective conduit for the initial inhalation then exhalation of gases to and from the lung while simultaneously performing multiple other functions, e.g., eating, drinking, speaking, etc. With respect to inhalation, the nasopharynx and posterior pharynx warms the inspired gas close to body

temperature and humidifies it to a water vapor pressure of 47 mm Hg at 37°C. This aids in maintaining core temperature and protects the more delicate epithelia lining the lower airways from desiccation. The airway epithelium secretes mucus which coats the airway surface and maintains tissue hydration also serves to trap particulate matter, bacteria, and viruses. Mucus also contains a number of enzymes with antioxidant, antiprotease, and antibacterial properties [6].

Another important role of the airways and its mucus coat is the filtering of inhaled particulate matter by an elaborate defense system that takes advantage of the air-flow characteristics of the upper and lower airways and their associated epithelium. There are three mechanisms at work to produce mechanical filtering. The first, inertial impaction, is capable of trapping particulates larger than 10 μm by virtue of the turbulent flow, mucus lining the passageways, and complex structure. It accomplishes this task in minutes with mucus and saliva eventually swallowed. The bifurcating and branching tracheobronchial tree slows the gas flow until it becomes more laminar. Particulates impact the airway wall according to particle size (sedimentation). Normally the particles, bacteria, etc. trapped in the mucus at this level are transported cephalad by the constant motion of the cilia, an apical feature of the respiratory epithelium, at a rate of approximately 2.5 mm/min in the bronchi but over 5 mm/min in the trachea [7]. Lower airway mucus is usually cleared in about 24 h although this can be drastically retarded in disease states such as cystic fibrosis or chronic bronchitis or conditions altering ciliary function or growth, e.g., smoking [8]. The filtering processes appear effective down to particles approximately 0.01 μm in diameter.

The Cough Reflex

An essential protective function of the respiratory system for expelling secretions and foreign bodies from the respiratory tract is the cough. The cough is a complex maneuver that is either voluntary or triggered by stimulation of airway irritant mechanoreceptors diffusely distributed throughout the larynx, trachea, and bronchi, especially the carina. Irritant chemoreceptors are distributed more diffusely in the distal central airways and at airway junctions, where noxious vapor particles are more likely to rain out on the epithelium. The vagus nerve serves as the primary afferent limb of the cough reflex but the efferent limb encompasses the motor input to the phrenic, intercostals, other spinal motor neurons to the accessory respiratory muscles and the vagal nerves to the larynx and pharynx.

There are several acts involved in generating an explosive flow of air and material out of the airways. The first is an exaggerated inspiration through a widely abducted glottis to achieve a high lung volume, which may be as high as 50% of vital capacity. By enlarging the intrathoracic volume, this produces a lengthening in the expiratory muscles and improves their length-tension relationship allowing greater

force generation. The second compressive phase begins with rapid adduction of the glottis simultaneous with the onset of expiratory muscle contraction. Glottic closure is accentuated by the tight adduction of the supraglottic ventricular folds. This phase lasts only hundredths of a second but is sufficient to produce a coordinated compression of the alveolar gas and increase in the intrathoracic pressure, briefly as high as 300 cm H₂O [4]. Abrupt initiation of the final expiration phase occurs with glottic release of this pressure producing nearly a subatmospheric drop in central airway pressures accentuating the pressure gradient from the continually rising alveolar and pleural pressures as a consequence of expiratory muscle contraction. An additional effect is dynamic compression of the airways which increases airflow velocity in relation to the volume of air expired per second. The total effect is a shearing force across the surface of the mucus-covered airway epithelia and mucus expulsion.

Clinical Issues

Airway Obstruction

Patients with tracheal or laryngeal mass lesions and those with vocal cord dysfunction can have significant flow resistance during inspiration and/or expiration depending on the intrathoracic vice extrathoracic location of lesions. High air flow rates through the site of the restrictive lesion can accentuate the increase in airway resistance. Less obvious is the effort-dependent dynamic compression that can occur in those portions of the airway that lie on either side of the lesion during the period of high flow [9]. Attempts to generate high flows create the greatest Bernoulli effect (acceleration-induced negative pressure) on the surrounding structures and can result in airway narrowing. This has clinical importance in managing patients pre- and postprocedure for laryngeal or tracheobronchial resections. Slow, easy breathing is more suitable than rapid, forced breaths; therefore judicious use of a sedative medication in addition to good postoperative pain management may improve gas exchange. This scenario is in contrast to that of patients with primary muscle weakness of the upper airway musculature either from residual neuromuscular blockade, general anesthesia, myasthenia, or extrapyramidal disorders [10]. These conditions require mechanical support until strength can be recovered or optimized.

Nebulized Medications

The features of the upper airway also impact the design and utility of multidose inhalers and medication nebulizers. Typically less than 30% of aerosolized drug with an average droplet size of 0.5 μm ends up in the lungs [11]. Even aerosolizing chambers attached to endotracheal tubes or ventilator circuits provide only a marginal improvement in efficiency at delivering drug to the distal airways.

Tracheobronchial and Respiratory Anatomy

Tracheal and Bronchial Structure

The trachea originates at the cricoid cartilage (opposite vertebra C6) and extends approximately 12 cm (females) to 14 cm (males) to terminate in a bifurcation (carina) at the T4/5 vertebral level (second intercostal space, the angle of Louis). It is about 22 ± 1.5 mm (males) to 19 ± 1.5 mm (females) in diameter and consists of 16–20 U-shaped cartilaginous “rings” that are closed posteriorly by fibrous tissue and a longitudinal smooth muscle band or trachealis muscle.

The right main bronchus is wider (14–17.5 mm), shorter (1.4–1.8 cm), and more vertical than the left. The right main bronchus gives off the upper lobar bronchus then continues on as the bronchus intermedius giving off the right middle lobar bronchus and right lower lobar bronchus at the hilum of the lung at T5. The azygos vein arches over it from behind to reach the superior vena cava. The right pulmonary artery lies first inferiorly and then anterior to the bronchus intermedius. The left main bronchus ranges an average of 4.4–4.9 cm in length and 13–16.5 mm in diameter. It passes inferiorly and laterally below the aortic arch, anterior to the esophagus and descending thoracic aorta to reach the hilum of the lung opposite T6. At this point it first lies behind and then slightly below the left pulmonary artery in its course. These dimensions can be quite variable among individuals and chest pathology can drastically change the anticipated relationships. We recommend always consulting available computed tomograms of the chest prior to any thoracic procedure to provide the anesthesiologist with more appropriate dimensions and structural relationships in their patient.

The lobar bronchi (right upper, right middle, right lower and the left upper, left lower) diverge into their segmental bronchi that can be readily visualized during flexible bronchoscopy (Table 4.1). The right upper lobar bronchus gives off three segmental bronchi (apical, anterior, posterior), the

right middle lobar bronchus splits into two segmental bronchi (lateral, medial), and the right lower lobar bronchus diverges into the superior segment with the basal segmental bronchus immediately diverging into four additional segments (medial basal, anterior basal, lateral basal, posterior basal) for a total of ten segmental branches on the right. The left upper lobar bronchus splits into the superior division with “3” segments (a “fused” apical-posterior, anterior) and the inferior division or lingual with two segments (superior lingular, inferior lingular). The left lower lobar bronchus branches into four lower segmental branches (superior, another “fused” anteromedial basal, lateral basal, posterior basal) for a total of “10” segments on the left (see also Chap. 16, Fig. 16.1a, b for CT reconstructions of the tracheo-bronchial anatomy). Note that segmental nomenclature can vary in the literature.

Respiratory Airways and Alveolar Histology

The airways continue to diverge into smaller and smaller diameter conduits until one arrives at the bronchioles with diameters less than 0.8 mm. At this level the airways lose all remnants of cartilage and begin the transformation from purely conducting airways to those described as respiratory bronchioles. Respiratory bronchioles eventually diverge into the final four generations of alveolar ducts which then consist primarily of openings into the terminal alveolar sacs. In the descriptive model of E.R. Weibel, the trachea branches into 23 generations of pulmonary airways. The first 15 generations serve as conducting airways and the subsequent 8 generations become sufficiently thin-walled to allow some degree of gas exchange and bear the moniker, acinar airways. One clinical aspect of this geometric progression of increasingly narrower airways (and blood vessels) by divergence and multiplication is that the overall cross-sectional area and therefore resistance to gas flow (or blood flow) becomes markedly less compared to the resistance of the individual airway (or blood vessel). This has an important impact on distribution of gas and blood flow, flow velocity, and, hence, transit time through key areas of gas exchange.

The trachea interior is lined with ciliated columnar epithelium, Goblet cells responsible for mucus production, and with interspersed specialized chemical and tactile neuroreceptors. This transitions from pseudostratified columnar epithelia in the larger bronchi to a thinner cuboidal ciliated variety in the small bronchi. The airway epithelium and submucosa also contain lymphocytes, mast cells, and a variety of neuroendocrine cell types. The next layer consists of circumferential bands of smooth muscle cells and a connective tissue layer containing submucosal glands and plates of cartilage (replacing the solid cartilage rings in the very large airways). The outermost layer is a loose adventitial shell with lymphatic vessels, sympathetic and parasympathetic nerves, and nourishing blood vessels.

The respiratory bronchioles empty into a pulmonary acinus, which has the appearance of a cluster of grapes on a network of stems. Each pulmonary acinus may contain multiple alveolar ducts communicating with 2,000 alveoli

TABLE 4.1. Bronchopulmonary segments.

Right lung	Left lung	
<i>Upper lobe</i>	<i>Upper lobe</i>	
Apical 1	Superior division	
Anterior 2	Apical + posterior	1+3
Posterior 3	Anterior	2
	Inferior division – lingula	
	Superior lingular	4
	Inferior lingular	5
<i>Middle lobe</i>		
Lateral 4		
Medial 5		
<i>Lower lobe</i>	<i>Lower lobe</i>	
Superior 6	Superior	6
Medial basal 7	Anteromedial basal	7+8
Anterior basal 8	Lateral basal	9
Lateral basal 9	Posterior basal	10
Posterior basal 10		

arranged in a ring-like, honeycomb network. The alveolus is considered the primary site of gas exchange between the blood and gas in the lung. The alveolar septa are about 5–8 μm thick and are opposed by an alveolar surface on either side with the alveolar capillary bed sandwiched inside. The walls of the alveoli are extremely thin, between 0.1 and 0.2 μm , a feature that promotes rapid equilibration of gas by diffusion with the pulmonary capillary blood. In addition, gas can exchange between alveoli through pores of Kohn. There are approximately 300 million alveoli in the human lung which provides an extraordinary surface area for gas exchange (70 m^2).

There are three major cell types found in the alveolus: alveolar type I, alveolar type II, and alveolar macrophages. However, there are others found under certain conditions in the lung, e.g., inflammation. Alveolar type I cells are a squamous epithelium class that cover most of the alveolar surface. These nucleated cells have few cytoplasmic organelles and a sparse cytoplasm splayed out in sheets over the alveolar surface forming a thin barrier between the air space and the pulmonary capillary endothelium. Alveolar type II cells are fewer in number, somewhat spherical, and coated on its apical surface with microvilli. In contrast to type I cells, alveolar type II cells possess many organelles including multilayered granular structures called lamellar bodies. These lamellar bodies are considered the source of pulmonary surfactant, a lipoprotein coating the interior surface of the alveolus and capable of significantly reducing the surface tension of the alveolus air–surface interface. Surface tension reduction is considered an important physical mechanism to reduce any tendency for alveolar collapse at very low lung volumes.

The immune defenses of the lung are extremely important because of its relative exposure to the environment via the airways. There are a number of excellent reviews of the immune function of the lung but it is important to realize that there are many questions unanswered about how the lung responds to invasion and inflammation [12]. Yet from a clinical standpoint the pulmonary inflammatory response will greatly influence the perioperative management of the thoracic surgical patient. A few major defensive cell types residing in the alveolar spaces and interstitium are worth mentioning. Alveolar macrophages are derived from bone marrow monoblast precursor cells and migrate to the lung parenchyma [13]. Alveolar macrophages are free to move over the surface of the alveolus and phagocytize foreign material that enters the alveolus including bacteria and particulates. Macrophages are cleared either through the lymphatics or are carried up and expelled via the airways. Lymphocytes, largely T-lymphocytes, are widely distributed in the normal lung within paratracheal and hilar lymph nodes, in the interstitium of the bronchial tree as nodules or individual cells, in the alveolar walls, and on the surface of the alveolus [14]. They play a critical role in the lung's primary immune response to inhaled antigens. Under some pathologic conditions in the lung, it is becoming apparent that an exaggerated inflammatory response and the activity of these cells and

others may be harmful to the lung; the acute respiratory distress syndrome (ARDS) and emphysema are examples.

Innervation

The hilum of each lung serves as the entry point of the bronchi, pulmonary vessels, bronchial vessels, lymph vessels and nerves. The lungs receive their innervation from the autonomic nervous system with branches from the vagus nerves and upper thoracic sympathetic ganglia (primarily second, third, and fourth). The vagal and thoracic sympathetic ganglia form anterior and posterior pulmonary plexuses at the hilum. From there two main neural networks develop; one accompanies the bronchi, the peribronchial plexus, and the other associates with the pulmonary vasculature, the periarterial plexus. Virtually all afferent nerve fibers entering the CNS from the airways travel through the vagus nerve [15].

Neural Control of Respiration

Respiratory Centers

It is generally accepted that the medulla contains the respiratory centers within the brain that are responsible for coordinating numerous voluntary and involuntary inputs then generating the appropriate respiratory pattern to fulfill the ventilatory requirements [16]. Two anatomically distinct but extensively interconnected locations control the character of the respiratory pattern and the motor control over supporting structures. The dorsal respiratory group receives visceral afferent input from cranial nerves IX and X and is primarily concerned with the timing of the respiratory cycle. It is predominantly composed of inspiratory motor neurons.

The ventral respiratory group is a collection of slightly more dispersed nuclei that are involved in both inspiratory and expiratory phases of respiration. This respiratory center has numerous functions that include control over the musculature of the pharynx, larynx and tongue, the magnitude of inspiratory force, and control over expiratory muscle activity and timing.

These centers receive modulating input from a number of higher centers such as the pons, hypothalamus, and the cortex. But the respiratory centers also receive stimulatory and inhibitory inputs from peripheral chemoreceptors, pulmonary and extrapulmonary mechanoreceptors. Peripheral stimuli such as airway stretch, blood pH, and airway chemical irritation can influence depth and rate of respiration as well as cough and sneezing reflexes.

Neural Control of the Airways

Neural control of the airway smooth muscle is important in determining airway caliber and pharmacologic modulation of this input is clinically relevant. The main neurotransmitters identified are acetylcholine (ACh) that acts on several muscarinic

subtypes, epinephrine and norepinephrine acting on both α - and β -adrenergic receptors, and a variety of purported nonadrenergic, noncholinergic neurotransmitters such as vasoactive intestinal peptide (VIP), nitric oxide (NO), substance P, and neurokinin A acting via second messenger cascades to elicit a variety of responses. See Barnes [17] for a detailed discussion. Although some of these neurotransmitters can have nonpulmonary sources, it is now clear that airway parasympathetic and sympathetic nerves can release more than one class of neurotransmitter. The end terminals of parasympathetic nerves can release ACh, VIP, NO, and others that have inhibitory and excitatory properties on either the primary target end-organ or the presynaptic terminus to modify release of the primary neurotransmitter. Similarly, sympathetic nerves release norepinephrine but also may secrete substance P, neurokinin A, VIP, calcitonin gene-related peptide, cholecystokinin-octapeptide, etc. The effects of many of these substances on the airway diameter, mucus secretion, and blood flow are still to be defined.

Cholinergic nerve influence on the human respiratory system is mediated via a family of muscarinic receptors on airway smooth muscle. Five muscarinic subtypes have been cloned, but only four have been identified in the lungs. These are M_1 -, M_2 -, M_3 -, and M_4 -receptors, although only M_3 appears to be responsible for the contractile response on human airway smooth muscle [18]. M_2 receptors on the airway smooth muscle cells act through an inhibitory G protein to block adenyl cyclase activity and lower cyclic AMP concentrations. Its role is yet to be determined, perhaps opposing the effects of β_2 -agonists. However, M_2 -receptors are also found on the human cholinergic presynaptic nerve terminal and likely functional as feedback inhibition to the further release of ACh. Alterations in the sensitivity or function of these receptor subtypes have been implicated in several disease states, especially influenza, asthma, and emphysema.

Adrenergic innervation of the human airways is present but despite the fact that airway smooth muscle possesses both α - and β -adrenergic receptors, direct adrenergic bronchodilator activity has not been demonstrated in contrast to observations in many animal models [19]. It appears that the more dominant role of adrenergic nerve stimulation is in presynaptic modulation of ACh release from airway cholinergic nerves via prejunctional β_2 -adrenergic receptors. Of note, β -blockers can have a profound negative impact on asthma exacerbations and yet have minimal effect on the bronchial tone of normal individuals. The mechanism behind this clinical observation is not known but may reflect expression of the asthmatic disease genotype. The absence of α -adrenergic receptors on human airway smooth muscle suggests that neuronal and adrenal catecholamines act directly only on arterial smooth muscle in the lung.

Respiratory Muscles

Bulk movement of air into and out of the lungs occurs as a result of changes in intrathoracic pressure created by rhythmic

changes in the volume of the thorax. Expansion of the chest cavity occurs when three distinct respiratory muscle groups work in concert. The diaphragm, intercostal muscles, and the accessory muscles (sternocleidomastoids, scalenes) are controlled by the respiratory centers of the brain to contract in a rhythmic pattern designed to carefully match ventilation to gas exchange requirements. The abdominal musculature (rectus abdominis, external oblique, internal oblique, and transversus abdominis) can be recruited when more force is required for exhalation, although abdominal muscle tone may stabilize the rib cage during inspiration as well.

Inspiration

The diaphragm is unique in that its muscle fibers radiate from a central tendinous structure to insert peripherally on the ventrolateral aspect of the first three lumbar vertebrae and on the aponeurotic arcuate ligaments, and the costal portion inserts on the xiphoid process and the upper margins of the lower six ribs. Its motor innervation is solely from the right and left phrenic nerves which originate from the third, fourth, and fifth cervical nerve roots. In the relaxed state it forms a pronounced “dome” that closely apposes the chest wall for some distance before arching across. Contraction of the diaphragm causes a large caudal displacement of the central tendon resulting in a longitudinal expansion of the chest cavity. Simultaneously, its insertions on the costal margins cause the lower ribs to rise and the chest to widen. This diaphragmatic motion is responsible for the majority of quiet respiration. Note that as the dome descends it must displace the abdominal contents caudally. The fall in pleural pressure and accompanying lung expansion produce an increase in abdominal pressure and some outward movement of the abdominal wall. The supine and Trendelenburg positions or surgical retractors can significantly impact this abdominal motion especially in the morbidly obese necessitating controlled ventilation under anesthesia.

The intercostal muscles are thin sheet-like muscles with origins and insertions between the ribs. The internal intercostal muscles have their fibers oriented obliquely caudad and dorsally from the rib above to the rib below. The external intercostal muscles have their fibers oriented obliquely caudad and ventrally from the rib above to the rib below. All intercostals are innervated by the intercostal nerves running in the neurovascular bundle under the inferior lip of each rib. The contraction of the external intercostals produces an inspiratory action by elevating the upper ribs to increase the anteroposterior dimensions of the chest in a “well pump-handle” motion. The lower ribs are also elevated by virtue of the force applied and their point of rotation to increase the transverse diameter of the thorax. The internal intercostals apply their force in such a direction as to rotate the ribs downward, decreasing the thoracic anteroposterior dimension to aid in active expiration. In general, the intercostal muscles do not play a major role in quiet respiration, but do in exercise or other conditions requiring high levels of ventilation.

The principal accessory respiratory muscles are the sternocleidomastoid and scalenes. The scalene muscles originate from the transverse processes of the fourth through the eighth cervical vertebrae and slope caudally to insert on the first two ribs. Their contraction during periods of high ventilatory demand elevates and fixes the cephalad rib cage during inspiration. Similarly, the sternocleidomastoid elevates the sternum and increases the longitudinal dimensions of the thorax.

Expiration

Expiration is a passive process in quiet breathing and is largely the response to relaxation of the inspiratory muscles and the balance of forces generated by the elastic recoil of the lungs and chest wall. When high levels of ventilation are required as in exercise or if airway resistance increases as in exacerbations of asthma, the expiratory phase becomes an active process with forceful contraction of the rectus abdominus, the transverse abdominus, and the internal and external oblique muscles. The contraction of the abdominal musculature retracts the abdominal wall and pulls the lower ribs downward which increases intra-abdominal pressure and accelerates the cephalad displacement of the diaphragm during exhalation. The internal intercostal muscles depress the rib cage and provide a minor contribution to forced expiration. Innervation of the abdominal musculature is from thoracic nerves 7 through 12 and the first lumbar nerve. These nerves are commonly affected by epidural anesthesia and thus can impact cough and other forced expiratory maneuvers.

Like most skeletal muscles, the diaphragm and intercostals muscles are a heterogeneous mix of fiber types, containing between 40 and 60% slow-oxidative (Type I) fibers. The human diaphragm probably has between 49 and 55% Type I fibers, the remainder a mix of the “faster-high activity” Type IIA and IIB fibers [20]. The types of skeletal muscle fibers seem to be distributed fairly evenly throughout the diaphragm. Of note the respiratory muscles retain the ability to adapt to stress and training. This includes responses to lung pathology which might seem maladaptive. Emphysema is a good example. The diaphragm undergoes changes at the sarcomere level, physically “losing” contractile units as hyperinflation of the lungs leads to increasing thoracic dimensions and “flattening” of the diaphragm [21]. It is proposed that loss of sarcomeres in series with the central tendon helps to restore the mechanical advantage of the optimal length-tension relationship for the muscle.

The Respiratory “System”

The Pleural Pressure

The lungs and chest wall move together as a system. This is made possible by the enclosed, air-tight thoracic cavity

where the outer surface of the lungs and its visceral pleura are in close proximity to the parietal pleura covering the chest wall and mediastinal structures. Changes in the intrathoracic volume are only possible because the inside of the lung is in continuity with the ambient atmosphere outside the thorax via the trachea and pharynx. The intimate contact between the layers of pleura is maintained by a negative intrapleural pressure generated in part by the intermolecular forces of the pleural fluid excluding gas from this space. This lubricating fluid allows freedom of the pleural layers to slide over one another but highly resists separation of the layers much like two panes of glass with a thin layer of water between them. Deforming forces are thereby directly and reliably transmitted between chest wall and lung and allows for a unified motion.

Normally the intrapleural pressure is about $-5 \text{ cm H}_2\text{O}$ when the respiratory system is in a “resting configuration or equilibrium state” but it can vary significantly. Recoil of the chest wall either outward or inward as with active exhalation, changes in elastic recoil of the expanded or contracted lung, diaphragm position, and body position (gravitational effects) will summate to define the magnitude of the intrapleural pressure (Fig. 4.3). Pathologic conditions such as the introduction of air or blood into the intrapleural space can rapidly disrupt this relationship leading to a compromise in respiratory function but also interfere with cardiovascular function. Examples of disruption of the intrapleural space would be a pneumothorax, a large empyema or pleural effusions, or a tension pneumothorax.

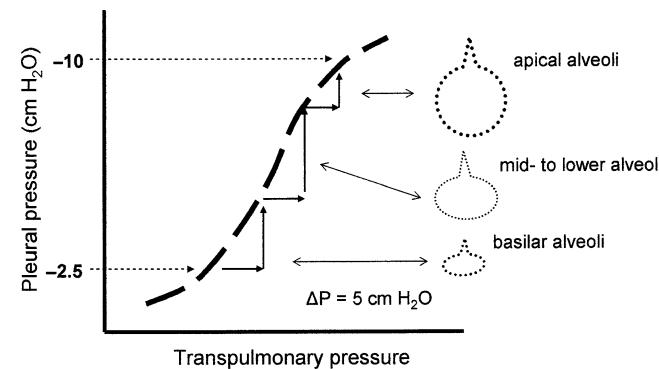


FIG. 4.3. The static relationship between the transpulmonary pressure (alveolar pressure – pleural pressure) and the pressure in the pleural space. Pleural pressure is normally negative relative to atmospheric pressure. The gradient is small at the base of the lung (P_{pl} least negative) but larger at the apex (P_{pl} most negative) because of the recoil pressure of the elastic lung tissue. This disparity results in larger alveoli at the apex than the dependent alveoli at the base. When atelectasis develops the alveoli are collapsed, a condition frequently seen in patients postthoracotomy even when sitting upright. As a result a given change in transpulmonary pressure produces the largest change in volume (and pleural pressure) where the alveoli sit on the steepest portion of this curve.

Lung Volumes

Clinical pulmonary physiology is based in part upon a common nomenclature of the measured lung volumes during a variety of respiratory maneuvers. Mastering this language facilitates effective communication across all disciplines within medicine and surgery. First, most lung volumes and capacities are measured by a device referred to as a spirometer. Spirometry and other associated measurement techniques have combined to define four major subdivisions of *lung volume*: (1) residual volume (RV), (2) tidal volume (V_T), (3) expiratory reserve volume (ERV), and (4) inspiratory reserve volume (IRV). These four lung volumes then can be combined to define the clinically useful four *lung capacities*: (1) total lung capacity (TLC), (2) vital capacity, (3) inspiratory capacity (IC), and (4) functional residual capacity (FRC). These terms and relationships are defined in Table 4.2. Details of their measurement are described in Chap. 2.

Differences in individual lung volumes are related to a large extent by body habitus, in particular, height. However, since TLC is influenced by lung and chest wall elastic recoil properties, inspiratory muscle strength, and body position, many conditions can alter its measurement. As an example, a “standard young adult male of average height” would likely have a TLC of about 6.5 L, of which 1.56 L is RV. Therefore his vital capacity would be about 5 L. However, the magnitude of the RV is a balance between expiratory muscle strength and the outward recoil of the chest wall at complete active exhalation. Although these predominantly static measurements are made without any confounding flow-resistance factors, “dynamic compression” of the airways from either extreme expiratory effort or loss of structural integrity with aging does occur and will increase lung RV. The lung volume at the end of a spontaneous exhalation during quiet breathing, the FRC,

marks a passive balance between the opposing elastic forces of the lung and the chest wall, i.e., the resting volume of the respiratory system. At this lung volume, airway pressure is zero (or equal to ambient atmospheric pressure); there is no pressure gradient between the inside of the alveoli and the mouth and therefore no air flow.

Dynamic Aspects of the Respiratory System

The Pressure–Volume Relationship

Both the chest wall and lungs are elastic structures and each has unique physical properties that define this elasticity. As elastic structures, the lungs and chest wall will return to their original configuration when deforming forces are removed. The equilibrium positions or volumes are not the same for the lung and chest wall. In fact it is possible to define the relationship between volume of the lung or chest wall (thoracic cavity) and a deforming pressure independently under experimental conditions. The static pressure–volume curve for an isolated lung is compared to that of a chest wall in Fig. 4.4. Note that the equilibrium position of the lung is at or near RV. To sustain any lung volume above this point requires the application of a distending force. The lung will recoil with an equal and opposing force. At all volumes above RV, the lung tends to recoil inwards as indicated by the positive pressure or distending force required (x-axis). On the other hand the equilibrium position of the chest wall is at a relatively large volume, estimated at approximately 60% of the TLC. To attain any “chest wall volume” above this point requires active inspiratory muscle force and likewise to decrease the volume below this point requires a significant input of expiratory muscle force. The thick solid line shows a summation of the two individual curves to define the static volume–pressure relationship for the total respiratory system. The recoil pressure of the respiratory system (P_{rs}) is defined as the algebraic sum of the individual recoil pressures of the lung (P_L) and the chest wall (P_{cw}).

$$P_{rs} = P_L + P_{cw}.$$

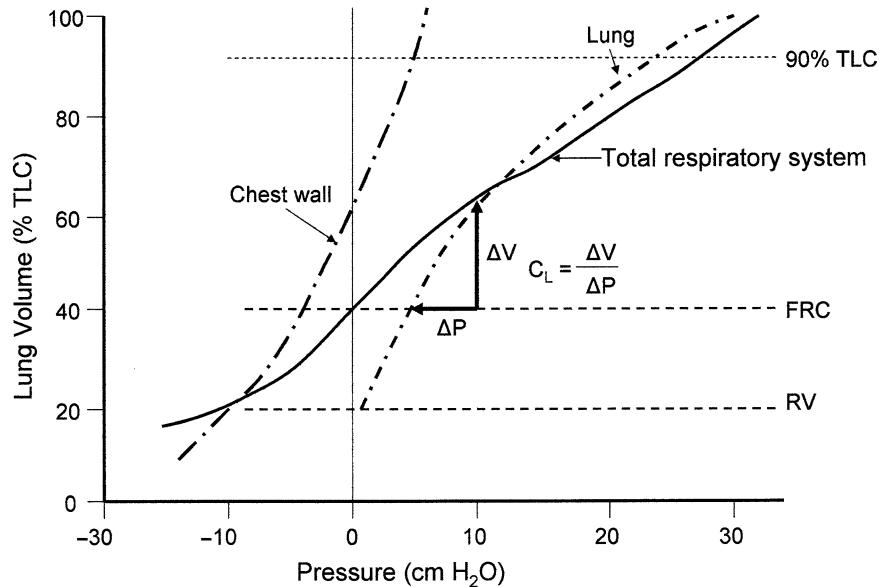
The volume at which the P_{rs} is zero is the relaxation volume (V_{rx}) of the respiratory system. In the normal healthy individual during quiet breathing, the volume of the lung at end of expiration (FRC) approximates the V_{rx} . However, under different circumstances, FRC may deviate from V_{rx} significantly. Numerous static factors such as posture, respiratory muscle tone, body habitus, and other external forces may reduce end-expiratory lung volume while dynamic mechanisms such as dynamic airway compression or asthma may increase it.

Postural influences on the pressure–volume relationship of the respiratory system are primarily related to gravitational forces on the abdominal contents. In the erect posture the downward pull of gravity displaces the abdominal contents

TABLE 4.2. Lung volumes and capacities.

Lung volumes	Definition
Tidal volume (V_T)	Air volume inspired and expired during a relaxed breathing cycle
Residual volume (RV)	Volume remaining in the lung after a maximal expiratory effort
Expiratory reserve volume (ERV)	The volume of air that can be forcibly exhaled between the resting end-expiratory volume and RV
Inspiratory reserve volume (IRV)	The volume of air that can be inspired with maximal effort above the normal resting end-expiratory position of a V_T
<i>Lung capacities</i>	
Vital capacity (VC)	The amount of air that can be exhaled from the point of maximal inspiration to the point of maximal expiration [IRV + ERV]
Total lung capacity (TLC)	Total volume of air in the lungs after a maximal inspiration [IRV + ERV + RV]
Functional residual capacity (FRC)	Amount of air in the lung at the end of a quiet exhalation [ERV + RV]

FIG. 4.4. Static pressure–volume curves of the respiratory system. The isolated chest wall pressure (P_{cw}) – thoracic cavity volume curve (large dash-dot line) crosses the zero pressure or equilibrium point at approximately 60% of TLC. The isolated lung pressure (P_L) – volume curve (small dash-dot line) approaches its equilibrium point at about 20% TLC or RV. Note that P_{cw} can be positive (force provided by contraction of the inspiratory muscles to achieve TLC) or negative (even greater force exerted by expiratory muscles to collapse the chest wall to reach RV). The algebraic summation of the chest wall and lung compliance ($\Delta V/\Delta P$) curves defines the static pressure–volume relationship of the total respiratory system (solid line). Note that in the totally relaxed state the balance between outward recoil of the chest wall and the inward recoil of the lung is at a lung volume (V_{rx}) that usually approximates functional residual capacity (FRC).



and tends to exert an inspiratory action on the diaphragm. In contrast, the upright posture affects the rib cage in a manner more like expiration, with gravity pulling the rib cage inward and downward. In the supine position, gravity exerts a small expiratory action on the rib cage but a more pronounced expiratory action on the abdominal contents and diaphragm. The pressure–volume curve for the chest wall is shifted to the right (i.e., produces less opposition to the inward recoil of the lung) and results in a shift in the V_{rx} and hence, FRC to smaller volumes (in normal individuals about 10% or more). The Trendelenburg position can emphasize this decrease in FRC by an additional 10% of TLC. This fact should be kept in mind when a patient is emerging from anesthesia following surgery in the supine or Trendelenburg position.

Lung Compliance, Lung Volume, and Dynamic Modifiers

Healthy adults with relatively stiff chest walls or low chest wall compliance (C_{cw}) tend to breathe near their relaxation volumes or FRC because the respiratory system is most efficient when under these conditions. In other words, the necessary transpulmonary pressure gradient (ΔP) that must be generated to produce an adequate resting V_T (ΔV) is optimized on the steeper slope of this pressure–volume relationship to require the least amount of work of breathing (WOB). The slope of this relationship defines the respiratory system compliance (C_{rs}). The compliance of the respiratory system is calculated in a similar fashion to P_{rs} . Since the pressure (at a given volume) is inversely proportional to compliance, the total compliance of the respiratory system (C_{rs}) is the algebraic sum of the reciprocals of the compliance of the lung (C_L) and the chest wall (C_{cw}). Therefore the equation is as follows:

$$1/C_{rs} = 1/C_L + 1/C_{cw}.$$

C_{rs} is normally in the range 50–80 mL/cm H₂O. Examples of pathologic conditions that alter compliance are pulmonary fibrosis (a decrease in lung compliance) and scoliosis (a decrease in chest wall compliance) through its effect on the spine and rib cage. To sustain the respiratory system at high lung volumes is disadvantageous from a mechanical standpoint and requires a considerable increase in WOB to balance the increased elastic chest wall and lung components. A secondary factor establishing the FRC is the interplay of dynamic factors [22]. During quiet breathing, there is sufficient time for passive emptying of the lungs. However, at high rates of ventilation during exercise or when emptying is delayed because of obstruction to flow, end-expiratory volumes may be determined more by dynamic factors rather than a static equilibrium. In obstructive lung diseases, despite the general increase in C_L by destruction of the alveolar architecture and decline in elastic recoil, the increase in V_{rx} (FRC) is as much a reflection of effort-dependent dynamic airway compression and expiratory flow limitation. Therefore, dynamic factors can play an important role in setting the equilibrium point for the volume of the respiratory system and FRC.

The notion that dynamic factors can impact FRC is an important one that influences not only normal physiology but thoracic pathology and artificial conditions such as general anesthesia and mechanical ventilation. Dynamic FRC is determined by the balance between two major factors: the time available for expiration (t_E) and the rate of lung emptying or flow. The expiratory time constant (τ), which in its simplest form is the product of airway resistance to flow (R_{aw}) and compliance (C_{rs}). As an example, neonates have an increased R_{aw} because of the small diameter of their airways and have a highly compliant chest wall (increased C_{rs}) due to their underdeveloped rib cage and musculature. Thus τ , which equals ($R_{aw} \times C_{rs}$), is relatively prolonged. If the ratio t_E/τ is less than 3, dynamic

FRC exceeds V_{ex} and airway pressure at end-expiration does not reach zero. Therefore there is incomplete expiration down to V_{ex} and retention of air occurs. This phenomenon continues to about 1 year of age whereupon sufficient maturity of the respiratory system produces a reduction in τ and increase in t_{e} to favor the normal adult pattern [23].

The same “air trapping” process can occur in adult individuals with prolonged expiratory times as a result of airway obstruction from COPD, asthma, or external airway compression from masses, for example. Incomplete expiration may occur during either spontaneous or mechanical ventilation. When describing a mechanically ventilated patient, the condition is referred to as “dynamic hyperinflation” and reflects a measurable increase in airway pressure above the normal zero pressure at end-expiration. In the literature this has often been referred to as “intrinsic PEEP” and reflects the pulmonary end-expiratory pressure produced by the elastic recoil of the respiratory system at the higher lung volume.

Distribution of Ventilation

Ventilation is not homogeneous in the lung due to a number of factors, some of which still remain controversial. The most frequent explanation for this nonuniformity is the effect of gravity and the balance of all of the previously mentioned forces acting on the lung and chest wall. In the upright posture, the greatest vertical height is attained by the lung. Because the lung consists of a honeycomb of interconnected thin-walled sacs and airways and holds a considerable volume of blood within the blood vessels interspersed within its structure, it has mass that is acted upon by gravitational forces. Gravity will tend to favor blood flow to the dependent portions of the lung, and therefore its weight will add to the weight of the lung tissue. This has multiple effects. First since the elastic lung septae are all interconnected, they distribute this force throughout the lung. The tendency for the lung to retract away from the chest wall at its apex creates a more negative (sub-atmospheric) pleural pressure than the pleural pressure at the lower dependent portions of the lung where its weight reduces the magnitude of the negative pleural pressure [24]. The gradient of pleural pressure from the lung apex to its base has been estimated at 0.4 cm H₂O per each centimeter of vertical height. Second, the increased stretch on the alveoli at the apex of the upright lung creates regions of larger, more inflated alveoli that become progressively smaller as one moves closer to the dependent lung base (Fig. 4.3). A consequence of this apical alveolar enlargement is to decrease compliance and create an inhomogeneous distribution of air within the lung during a breath at FRC; greater distribution of the breath to the base as opposed to the apex [24, 25]. Obviously, one might expect less of a transpulmonary pressure gradient from nondependent to dependent portions of the lung when supine or prone as compared to the upright position. In addition, the bronchi are supported by the radial traction of the surrounding lung parenchyma. Airway caliber will increase as the lung expands

and contract when the lung shrinks significantly impacting airway resistance. At very low lung volumes, the small airways may close completely, a condition frequently seen at the very base of the lung where it is less well expanded. Also, the rate of inspiration directly impacts the homogeneity of gas distribution. At high inspiratory rates, air is distributed more evenly throughout the lung than at very slow rates [26].

In summary, numerous studies using a variety of tracer gases (e.g., N₂, He, ¹³³Xe) to measure alveolar gas washout have demonstrated that inspired gas distribution is inhomogeneous [25]. In the ideal, upright individual, during a spontaneous breath, inspired gas will tend to preferentially enter those open alveoli near the base of the lung which are the most compliant. As the breath continues, the gas will enter the more apical, less compliant alveoli and any previously atelectatic basilar alveoli as they become recruited by the traction exerted by the remainder of the expanding lung. In other words, although the nondependent lung areas are more distended at FRC, a given transpulmonary pressure gradient generated during a normal breath produces a greater volume change and therefore ventilation, to the dependent areas. Review Figs. 4.3 and 4.4 for a graphical explanation of the underlying mechanism. Numerous factors are responsible for the distribution of ventilation and their potential impact in the thoracic surgical patient must be anticipated as body position, anesthetic gases, intravenous fluid shifts, surgical trauma, one-lung ventilation with positive pressure, and any broncho- or vasoactive drugs are introduced. These regional differences in ventilation are important in matching ventilation to perfusion for optimal gas exchange.

The Pulmonary Circulation

Anatomical Considerations

The lung circulation comprises two sources of blood flow; the pulmonary circulation from the main pulmonary artery and the smaller, bronchial circulation arising from the aorta. The pulmonary circulation dominates, by volume, and serves to deliver the mixed venous blood to the alveolar capillaries to facilitate gas exchange and to act as a large, low resistance reservoir for the entire cardiac output from the right ventricle. The bronchial circulation serves to provide nutritional support to the airways and their associated pulmonary blood vessels [27]. The bronchial circulation also provides a constant source of heat and moisture for warming and humidifying the inspired air. Of note, not all of the bronchial circulation drains into the systemic venous system. A small portion of the bronchial venous drainage mixes with the pulmonary venous drainage and contributes a small physiological shunt.

Pulmonary Hemodynamics

Despite receiving all of the cardiac output from the right ventricle, the pulmonary vasculature maintains a relatively low pulmonary blood pressure. The normal adult mean pulmonary artery pressure (P_{PA}) is between 9 and 16 mm Hg with systolic

P_{PA} between 18 and 25 mm Hg. Several features enable the pulmonary circulation to maintain this high flow at such low pressures. First, the pulmonary vasculature is extremely thin-walled with far less arterial vascular smooth muscle than its systemic counterparts. The result is a highly compliant reservoir capable of accommodating an average 3.2 L/min/m² blood flow at rest or 6–8 times that flow during exercise. Second, the total pulmonary vascular resistance (PVR) is quite low, on the order of less than 250 dynes/s/cm⁵. This minimizes the pressure work faced by the less robust right ventricle while still enabling the right ventricle to match the output of the left ventricle. PVR can change as a result of numerous factors, hypoxia, acidosis, mitral valve stenosis or regurgitation, left ventricular failure, primary pulmonary hypertension, or pulmonary emboli, to name just a few. PVR can be calculated using data from a pulmonary artery catheter as:

$$PVR = [(P_{PA} - PAOP) / CO] \times 79.9.$$

where PAOP is the pulmonary artery catheter occlusion pressure which is assumed to reflect the left atrial pressure, CO is cardiac output (L/min), and the factor, 79.9 converts from mm Hg/L/min to units of absolute resistance, dynes/s/cm⁻⁵.

Distribution of Perfusion

Gravity and Pulmonary Blood Flow

Blood flow within the lung is distributed in a nonhomogeneous fashion. Many studies have demonstrated this behavior although explanations vary [28–30]. The earliest studies used radioactive tracers injected into the bloodstream and measured the radioactive emissions by sandwiching the subject between two external arrays of scintillation counters. The most common tracer employed was xenon-133 which has an extremely low solubility in the blood so most of it rapidly moves into the alveoli during the first pass, i.e., little recirculation. The time to achieve a steady state in the lung after injection was estimated at 3–4 s. Data acquisition of a 30-cm scan of the chest could be completed in about 30 s enabling single breath-hold studies at different static lung volumes. The data were limited to a two-dimensional representation of the lung and failed to account for the very apex and base of the lung for technical reasons. Nonetheless the studies clearly showed a gradient of perfusion from the apex and increasing toward the base in the upright lung; presumably reflecting the effects of gravity [25]. However, more refined techniques using radioactive microspheres and advanced computerized three-dimensional imaging techniques have revealed that blood flow distribution is highly variable even in those portions of the lung at a uniform vertical height [31, 32]. Indeed it appears that there are “high-flow” and “low-flow” regions of the lung whose perfusion is only minimally altered by changes in body position. Several studies performed under zero-gravity [33, 34] and microgravity [35] support the notion that the whole-lung gravitational and postural changes

seen in blood flow distribution are primarily determined by shifts in the lung parenchymal density which are augmented by smaller gravitational contributions to individual alveolar flow within the dependent regions of the lung.

Architecture and Pulmonary Blood Flow

If gravitational influences fail to completely explain the heterogeneity of lung perfusion then other factors must be present. One popular concept is the role played by the branching pattern of the blood vessels. At each pulmonary vascular branch point, that proportion of the pulmonary blood flow that continues down each subsequent arterial branch is dependent upon its downstream resistance to flow. The progressive branching pattern of the blood vessels is assumed to be similar in geometry within each generation. However, the number of generations will be influenced by the size of lung region. This “fractal geometry” theory has been employed in a number of biological systems to analyze flow [36]. Indeed its use as a foundation to explain heterogeneity in the distribution of gas and blood through generations of branching airways and vasculature has proven particularly useful [37, 38].

When ¹³³Xe blood flow studies are performed at different lung volumes in the same individual, a marked variation in the distribution occurs [39]. The greatest changes occur at the apex and base of the lung. Going from TLC to RV results in large drop in the percentage of blood flow to the base while a modest increase in the flow to the apex occurs at RV compared to TLC. One explanation for this pattern of regional blood flow is that, similar to the effects on airway resistance, traction exerted on the small arteries within the lung parenchyma decreases their resistance. The greater the traction, e.g., at high lung volumes, the lower the arterial resistance. However, to explain the improvement in apical blood flow at RV requires that we suppose that large lung volumes compress the alveolar capillaries and increase their resistance to flow. Therefore, there must be a balance between alveolar pressure effects on the alveolar capillaries and the interstitial traction effects on the extra-alveolar pulmonary arterioles. Figure 4.5 illustrates this concept of lung volume and vascular resistance of intra-alveolar and extra-alveolar blood vessels.

Regional “Zones of Blood Flow”

A common conceptualization of the effects of posture and hemodynamics on the distribution of blood flow within the whole lung, the “Zones of West” model, has been useful clinically. First described in 1964 by West and Dollery, the model describes the dependence of pulmonary perfusion upon the interaction between three basic pressures: alveolar pressure, pulmonary arterial, and venous pressures [25]. The notion of three (or four) “lung zones” dictated the blood flow through the acinus (see Table 4.3 and also Chap. 5, Fig. 5.10). In Zone 1, the alveolar pressure (P_A) is considered to be greater than both the arteriole (P_a) and venule (P_v) pressures thus creating

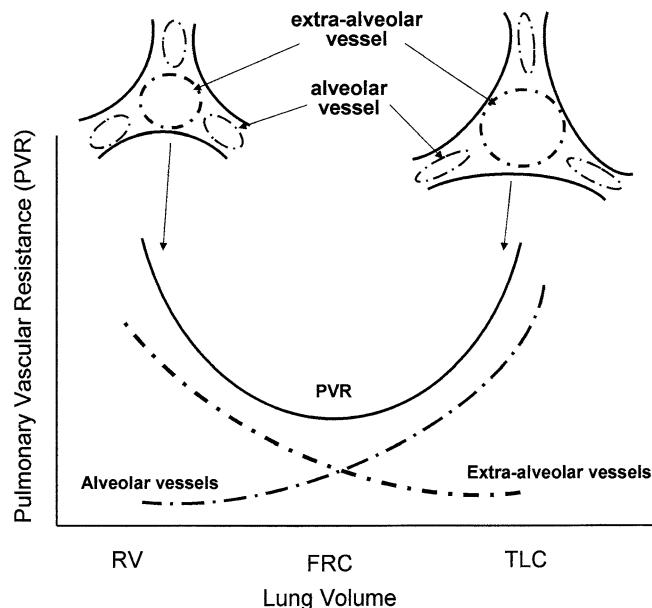


FIG. 4.5. Pulmonary vascular resistance (PVR) changes with lung volume. Small pulmonary blood vessels are affected by lung volume as a result of their location with relation to alveolar sac. Alveolar capillaries are most compressed between alveoli at high lung volumes, while extra-alveolar vessels are stretched by the radial traction of the lung elastic recoil. The relationship is just the opposite at low lung volumes. As a result total PVR is highest at both extremes of lung volume and has its nadir at FRC.

TABLE 4.3. Regional flow zones of the lung.

Zone	Pressure relationships	Blood vessels	Determinants of blood flow
1	$P_A > P_{pa} > P_v$	Collapsed	Minimal flow
2	$P_{pa} > P_A > P_v$	Intermittent patency	$P_{pa} - P_A$
3	$P_{pa} > P_v > P_A$	Distended	$P_{pa} - P_v$
4	$P_{pa} > P_{isf} > P_v > P_A$	Restriction	$P_{pa} - P_{isf}$

P_A alveolar pressure; P_{pa} pulmonary arteriole pressure; P_v pulmonary venule pressure; P_{isf} interstitial fluid pressure

a decreased transmural pressure favoring compression of the alveolar capillary and impeding blood flow (Fig. 4.5). Zone 1 (most nondependent region of lung) is considered to be fairly small in the spontaneously breathing individual but can enlarge during positive pressure ventilation. Zone 2 (a transition region between the most nondependent and dependent regions) is where the arteriole pressure (P_{pa}) is greater than alveolar pressure (P_A) but venule pressure (P_v) remains less than the other two pressures throughout most of the respiratory cycle. The net effect is a resistance to blood flow governed by the difference between P_{pa} and P_A . The transition is likely a gradual one and will vary throughout the respiratory cycle, especially when mechanical ventilation is employed. The size of Zone 2 will be subject to a wide variety of clinical conditions. The bulk of the normal lung is likely described by Zone 3

(dependent region of lung) where both arteriole and venule pressures are greater than alveolar pressure during all phases of the respiratory cycle such that blood flow is unimpeded and, presumably, gas exchange continues unabated. Finally, a Zone 4 has been proposed. It is that region where atelectasis or severe pulmonary interstitial edema has developed and results in blood flow determined by the difference between P_{pa} and the pulmonary interstitial fluid pressure (P_{isf}).

The pulmonary vasculature can best be viewed as a large branching tree with two components defining the distribution of blood flow within it. One component is the fixed structure that is the primary determinant of regional perfusion. However, superimposed on this fixed component is a highly variable component that is influenced by numerous local factors. While fractal geometry can explain properties of the fixed component, the variable component is less predictable and subject to both passive and active regional factors. Some examples of regional factors are recruitment and distension due to changing cardiac output and blood pressure, lung distension or vasomotion in response to HPV, shearing stresses, or pharmacologic interventions. The importance of all of these influences on ventilation and perfusion in the lung cannot be overstated. To optimize gas exchange requires the best possible “match” between alveolar ventilation and the delivery by the blood of CO_2 to the alveolus for removal and the absorption of O_2 for delivery to the body to sustain metabolism.

Ventilation to Perfusion Matching (The V_A/Q Ratio)

In a perfect world, the ventilation perfectly matches the perfusion in the lung. Therefore with a typical resting value of alveolar ventilation of 4 and 5.1 L/min for pulmonary blood flow, we could calculate a global ventilation to perfusion ratio (V_A/Q) of 0.8. However, as we have already discussed, the lung does not enjoy a homogeneous distribution of either ventilation or perfusion. A gradation exists between alveoli that are underventilated to those that are grossly underperfused. As expected the V_A/Q ratios will vary from zero where an alveolus is perfused but not ventilated to a V_A/Q ratio of infinity where there is no alveolar blood flow but the alveolus remains ventilated. Useful physiologic descriptors of these two extremes are “physiological shunt” for a V_A/Q ratio nearing zero and “physiological dead space” when the V_A/Q ratio approaches infinity. The prefix “physiological” connotes that physiologic events can be superimposed to create these conditions in contrast to fixed anatomical arterial-venous shunts or the non-respiratory airways, i.e., anatomical dead space.

In the healthy conscious individual, the expected shunt or venous admixture is only about 1–2% of the cardiac output. This degree of venous admixture is likely to produce an alveolar to arterial PO_2 gradient of about 7 mm Hg or less in someone breathing ambient air. However, the degree of venous

admixture has been shown to increase with age. Administration of 100% inspired oxygen can achieve acceptable P_aO_2 in the face of venous admixture up to about 30%. During most general anesthetics, an F_iO_2 of 40% is sufficient unless moderately severe shunting is present. Shunting developing during general anesthesia likely has two sources, atelectasis and redistribution of ventilation to regions of high V_A/Q ratio. The former can be corrected or significantly reduced by the application of PEEP. The latter may actually be worsened by PEEP. The end result will depend on the condition predominantly causing the increased venous admixture.

These conditions have significant consequences for metabolic homeostasis because of its impact on gas exchange. Alveoli with no ventilation will have a P_aO_2 and P_aCO_2 identical to that of mixed venous blood because the trapped alveolar gas will equilibrate with the CO_2 and O_2 levels in the mixed venous blood. Likewise for those alveoli ventilated but not perfused, the P_aCO_2 and P_aO_2 will be identical to the inspired gas since there is no blood to either add CO_2 or remove O_2 from the alveolus. Therefore for all alveoli with ratios in-between these extremes, their alveolar gas partial pressures will reflect the degree of both ventilation and perfusion. V_A/Q ratios have been measured under a variety of conditions and modeled to show a basic pattern in the normal upright lung under spontaneous respiration (see Fig. 4.6). Note that perfusion changes relatively more than ventilation as you progress from the lung base to its apex resulting in V_A/Q ratios ranging from 0.6 to 3.3 [40]. Even these ratios may not represent the extreme values in the upright lung since the apex and base of the lung do not lend themselves to accurate assessment for technical reasons.

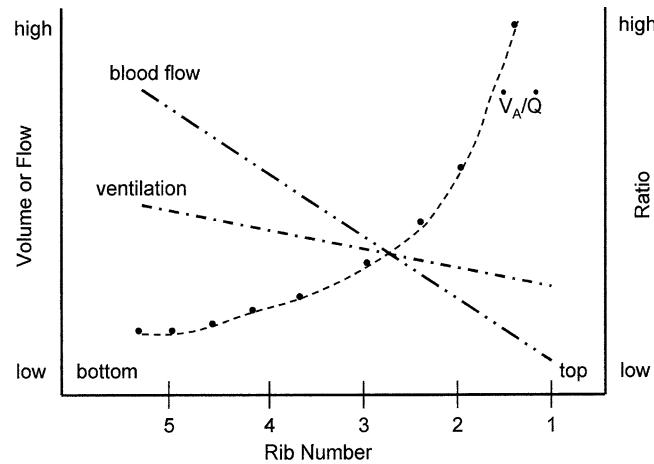


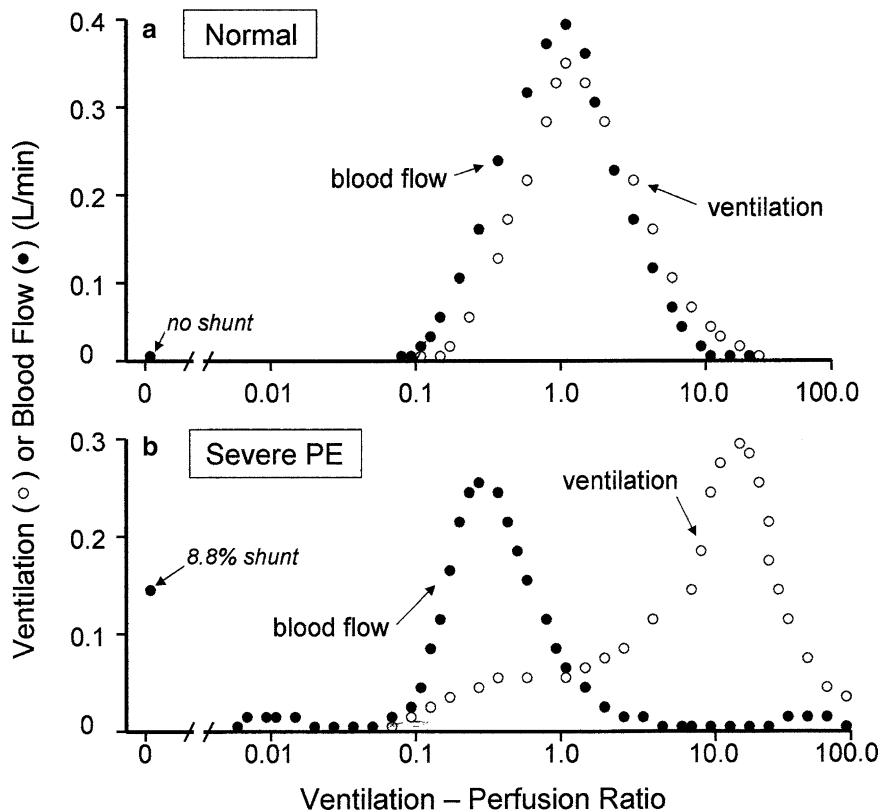
FIG. 4.6. General distribution of blood flow and ventilation and the ventilation-to-perfusion ratio as a function of distance from the base of the upright lung to its apex. Both ventilation and blood flow are significantly greater at the base of the lung than its apex. However, the relation is much steeper for blood flow than for ventilation. Therefore, the ventilation-perfusion ratio (V_A/Q) is greater at the apex or nondependent regions of the lung than the base or dependent regions of the lung.

One method that has been used extensively in the laboratory to detect and quantify the disparity between ventilation and perfusion in normal and diseased human lungs is the Multiple Inert Gas Elimination Technique (MIGET) [41]. Multiple tracer gases dissolved in a physiologic medium are infused intravenously for 30 min. The original mix included SF6, ethane, cyclopropane, halothane, ether, and acetone which are nonreactive with hemoglobin and possess a wide range of solubilities. After 30 min, mixed venous, arterial and mixed expired samples are taken and analyzed by gas chromatography for the arterial retention and alveolar excretion of each gas. Cardiac output and minute ventilation are measured. Each tracer gas has a linear dissociation curve and a single blood-gas solubility co-efficient. Plots of ventilation and blood flow vs. calculated V_A/Q ratio are derived for each gas. The composite V_A/Q distribution is fitted to 48 discrete compartments plus one for shunt ($V_A/Q=0$) and one for alveolar dead space ($V_A/Q=\infty$). Note the characteristic plots in Fig. 4.7. Figure 4.7a shows a normal subject characterized by a near-perfect match between the blood flow curve and the ventilation curve. But note that both distributions are bell-shaped curves supporting the notion of heterogeneity of both ventilation and perfusion in the normal lung. In comparison, Fig. 4.7b demonstrates a characteristic graph with a large degree of mismatch produced, in this case, by multiple pulmonary emboli. Note the significant physiologic dead space indicated by considerable ventilation to underperfused regions. In addition, there are large regions of perfusion to areas that are relatively underventilated producing areas in the lung of physiologic shunt. Finally, note the calculated shunt fraction of 8.8%; likely the result of pulmonary edema. It is also possible that under this pathologic condition, a portion of the cardiac output is passing through the lung through anatomic a-v shunts as well. These paths may become recruited when PVR increases as a compensatory mechanism to limit the increase in PVR or to accommodate gross increases in pulmonary blood volume as in congestive heart failure.

Hypoxic Pulmonary Vasoconstriction

HPV is an adaptive vasomotor response to alveolar hypoxia, which redistributes blood to optimally ventilated lung segments by an active process of vasoconstriction, thereby improving ventilation-perfusion matching. This is the major intrinsic mechanism of the lung to divert blood flow from pulmonary acini served by occluded or partially ventilated bronchioles to neighboring well-ventilated pulmonary acini. Such conditions can transiently develop under a number of conditions, micro-atelectasis, mucus plugging, edema or inflammation, for example. HPV provides for a rapid and reversible response to changing conditions in the local environment. The mechanism is most efficient when the adjustments are restricted to small distances between adjacent pulmonary acini or at most, bronchiole segments. It tends to be less effective when the involved areas become large such as whole lung segments

FIG. 4.7. Ventilation (open circles) or pulmonary blood flow (closed circles) as a function of computed ventilation–perfusion ratio (V_A/Q) using the MIGET. See text for details of the experimental method. (a) Normal distribution of ventilation, blood flow, and calculated V_A/Q ratios demonstrating a good match between alveolar blood flow and alveolar ventilation. (b) A characteristic plot in the presence of multiple pulmonary emboli. Note the dispersion of blood flow to regions of the lung with low V_A/Q ratios and the ventilation distributed to areas of high V_A/Q ratios. Ventilation is wasted presumably because of the obstruction of the pulmonary blood flow to many regions by emboli. The high calculated shunt of 8.8% likely reflects pulmonary edema and possibly the increased blood flow through anatomic arterial-venous shunts as a result of pulmonary hypertension (based on data from Wagner et al. [90]).



or lobes. When global hypoxia is present as in the fetus in utero, HPV mechanisms lead to very high pulmonary arterial pressures which divert blood through the foramen ovale and ductus arteriosus, a useful adaptation to life with a placenta. However, when alveolar hypoxia is global as upon ascent to high altitude, ARDS, hypoventilation syndromes, severe cystic fibrosis, or emphysema, HPV responses can be maladaptive and lead to pulmonary hypertension and potentially, right heart failure.

The molecular and subcellular mechanisms subserving HPV are a contemporary polemic. However, several aspects are well documented and are important to the clinician. We will focus on these in our discussion. Bradford and Dean [42] were credited with the first modern observation of HPV as a result of asphyxia in 1894 and noted the dichotomy between the vasodilatory response of systemic arteries and the vasoconstriction of pulmonary arteries by the same stimulus. Recognition of HPV as an important adaptive mechanism for ventilation–perfusion matching is attributed to Von Euler and Liljestrand [43]. They noted the vasoconstriction of small intrapulmonary arteries in response to hypoxia without hypercapnia; a response limited to the pulmonary circulation. Later it was shown that the predominant stimulus was an inspired hypoxic gas mixture and not hypoxemia per se. Initial animal experiments showed that if the normal alveolar O_2 partial pressure was maintained in the face of a hypoxic blood perfusate to the lung, minimal HPV occurred [44, 45]. However, subsequent studies have clearly demonstrated that a low mixed

venous PO_2 and therefore low pulmonary artery P_aO_2 will augment the HPV response to an hypoxic F_iO_2 but low pulmonary venous PO_2 has no effect [46, 47]. Indeed, as the size of the hypoxic lung increases, PVR increases, mixed venous oxygen tensions begin to fall, and the ability of HPV to shunt blood to the remaining well-ventilated lung becomes compromised. In fact if mixed venous PO_2 drops significantly, P_AO_2 in the ventilated alveoli drops sufficiently that the pulmonary perfusion pressure of those segments increases as well [46, 48]. Others have demonstrated that HPV remains intact despite chemical sympathectomy, bilateral vagotomy, and denervation of the carotid and aortic chemoreceptors [49, 50]. Finally, bilateral lung transplants in man retain their hypoxic pulmonary vasoconstrictive responses [51]. HPV is augmented by conditions and chemicals which globally enhance PVR such as acidemia, hypercapnia, histamine, serotonin, and angiotensin II to name a few.

The actual cellular oxygen sensor has yet to be determined. Current research appears to implicate the mitochondria of the pulmonary vascular smooth muscle cell as the main site [52, 53]. Numerous biochemical studies have indicated that selective interruption of the mitochondrial electron transport chain complexes can impair HPV. A unifying theme seems to be the hypoxia-induced change in the level of oxygen free radicals and hydrogen peroxide in the smooth muscle cell [54]. These changes affect the release of calcium from the sarcoplasmic reticulum and the voltage-dependent membrane conductance to potassium resulting in depolarization

and contraction of the smooth muscle; hence vasoconstriction [52, 53, 55]. There appears to be a two-step response to hypoxia with an immediate increase in PVR and pulmonary perfusion pressure occurring within minutes followed by gradual increase to a maximum that occurs over hours and can be sustained [56–58]. The response can be enhanced by hypercapnia and may involve decreased production of NO by the pulmonary epithelium and endothelium [56].

Clinical Applications

Anesthesia and Atelectasis

J.F. Nunn was one of the first to show that during anesthesia and spontaneous ventilation, gas exchange was altered by shunt and inhomogeneous V/Q ratios [59]. He concluded from his observations that a normal range of P_aO_2 could be maintained if the alveolar PO_2 (P_aO_2) was at least 200 mmHg which would require an F_iO_2 of at least 35%. Many have speculated that induction of general anesthesia lead to decline in oxygenation as a result of alveolar collapse (atelectasis), but it was an important observation by Brismar et al. [60] that demonstrated the regional collapse of lung. They were able to demonstrate using computed tomography that within 5 min of the induction of anesthesia, dependent edges of the lung developed an increase in density consistent with atelectasis. It is now accepted that this occurs in dependent lung regions in approximately 90% of patients who undergo general anesthesia using a wide variety of agents [61]. Epidural anesthesia may be the one modality that appears to cause very little atelectasis and no change in V_a/Q matching or oxygenation [62, 63].

Three basic mechanisms are currently implicated in the cause of atelectasis under general anesthesia. See the excellent review of the topic by Magnusson and Spahn [64]. The near universal finding of rapid lung collapse upon induction of anesthesia and the rapid reappearance after discontinuation of PEEP has led to the conclusion that atelectasis was due to compression of lung tissue rather than alveolar gas absorption behind occluded airways [60]. The fluoroscopic study by Froese and Bryan of the diaphragmatic motion of spontaneously breathing volunteers demonstrated that in the supine position the dependent portion of the diaphragm had the greatest cephalad displacement. Initiation of paralysis with neuromuscular blocking agents and positive pressure ventilation created a reversal of this motion with the nondependent or superior aspect of the diaphragm underwent the greatest displacement with each ventilated breath [65]. Others have confirmed and extended these observations using CT scans [66, 67]. It is now apparent that the geometry of the chest and diaphragm is altered under general anesthesia with greater relaxation of the chest wall and a marked cephalad displacement of the most dorsal portion of the diaphragm in end-expiration.

Absorption atelectasis can occur when the rate of gas uptake into the blood exceeds the rate of ventilation of the alveolus.

The extreme condition is total occlusion of an airway which isolates the alveolar gas in the distal alveolar and respiratory airways. The gas pressure within this compartment initially is nearly at atmospheric pressure. However, given that mixed venous blood continues to perfuse this area, and the fact that the sum of the gas partial pressures within mixed venous blood is subatmospheric, gas uptake from the occluded compartment by blood continues and the alveoli collapses [68]. Computer modeling has demonstrated that the rate of gas absorption from unventilated areas is dependent upon the initial F_iO_2 [69]. However, in many clinical situations the airways are not completely occluded but rather ventilation to an area becomes severely reduced. If the inspired V_a/Q ratio of a respiratory unit is reduced, a point is reached where the rate at which inspired gas enters the alveolus is exactly balanced by the gas uptake into the blood. If V_a/Q ratio drops below this critical equilibrium point, the volume of the alveolus declines and collapse ensues. Again this process is augmented by the presence of a high P_aO_2 and a rapid rate of gas uptake [70, 71].

Finally, loss of alveolar surfactant may play a role in alveolar instability at low alveolar volumes and collapse. The rapidity of alveolar collapse following alveolar recruitment maneuvers and discontinuation of PEEP has suggested that atelectasis per se may interfere with surfactant production. Therefore, atelectatic regions of the lung may be predisposed to recurrence of collapse because of reduced levels of surfactant, increased alveolar surface tension and, the aforementioned mechanisms, all contributing to reduced alveolar volumes.

Anesthesia and V_a/Q Matching

Of great interest to anesthesiologists, is the impact of their anesthetic or pharmacologic interventions on the pulmonary homeostatic mechanisms. A wide variety of drugs have been investigated with respect to HPV and V_a/Q matching. In general, volatile anesthetics do not have a large impact on HPV. However, volatile anesthetics could have a significant clinical effect in those patients with diseased lungs or poor cardiac function. Isoflurane can decrease cardiac output and is a potent vasodilator. As such it has been possible to demonstrate a concentration-dependent reduction of regional HPV by isoflurane during one-lung ventilation in experimental animals [72]. Domino et al. calculated that this increased the degree of shunt flow by approximately 4%. It is likely that this effect on blood flow and V_a/Q mismatch would be amplified in a thoracotomy patient with diffuse lung disease and with a significant preoperative fraction of cardiac output going to the nondependent lung. The newer volatile anesthetics cause less vasodilation but still produce some, albeit small, degree of shunt possibly through their general effects on cardiac output [73–75]. Studies in animals indicate that 70% nitrous oxide moderately diminishes the HPV response [76]. The general impression is that all volatile anesthetics can affect the HPV mechanism to some degree but rather it is their impact on the patient's general physiology that may warrant greater

consideration in their selection. When volatile anesthetics are compared with propofol or propofol and narcotic infusions, there appear to be only slight differences, none reaching statistical significance [75, 77, 78]. Intravenous drugs of most classes used in anesthesia such as barbiturates, opioids, benzodiazepines, and ketamine do not appear to have a measurable effect on the HPV response. However, these drugs can still influence hemodynamics in other ways which can impact blood flow through the lung. Therefore except for possible changes in emergence pharmacokinetics or pharmacodynamics, there are no known significant advantages of using total intravenous anesthesia over volatile anesthetics with regard to HPV in the thoracotomy patient.

The effects of thoracic epidural anesthesia or analgesia on HPV have not been as extensively studied. However, those animal studies examining the effects of thoracic epidural local anesthetics have not seen a significant blunting of HPV and any changes in shunt fraction are more likely to represent changes in global hemodynamics [79].

Nonanesthetic Drugs and HPV

In addition to volatile anesthetics, there are numerous drug classes that influence PVR and several have been shown to modify HPV directly. A partial list of common drugs that can affect the pulmonary vasculature are compiled in Table 4.4. Unfortunately, detailed pharmacodynamic studies are missing for many of these drugs which are commonly being used in patients. So it is quite difficult to extrapolate experimental findings to the clinical setting. Nonetheless the thoracic anesthesiologist must be aware of the potential effects of using vasoactive drugs in a perioperative setting where undesirable effects on HPV may be manifest.

Interventions to modify blood pressure or improve inotropic state can have direct effects on the pulmonary vasculature. Sodium nitroprusside, nitroglycerin, and hydralazine are potent vasodilators that can worsen P_aO_2 rapidly by reducing HPV, although preexisting vascular tone can influence the response [80, 81]. Attempts to improve the inotropic state of the heart, especially the right ventricle, with milrinone will concurrently vasodilate the pulmonary vasculature [82].

TABLE 4.4. Drug effects on PVR.

Decrease PVR	Increase PVR
Angiotensin II receptor blockers	α_1 -Adrenergic receptor agonists
ACE inhibitors	Almitrine
β_2 -Adrenergic receptor agonists	Angiotensin II
Calcium channel blockers	β -Adrenergic receptor blockers
Inhaled nitric oxide	Cyclooxygenase inhibitors
Milrinone	Histamine (H_1)
Nitroglycerin	Serotonin
Sildenafil	
Sodium nitroprusside	
Theophylline	
PGE ₁ and PGI ₂	

The improvement in cardiac output can enhance systemic O_2 delivery and mixed venous PO_2 so that the net effect on V_A/Q matching could be beneficial. Perioperative administration of inhaled NO, inhaled PGI₂, and sildenafil to control pulmonary hypertension and improve the right ventricular afterload will also modulate HPV [83, 84]. Fortunately, inhaled pulmonary vasodilators are more selective and theoretically are distributed to those better-ventilated lung regions to enhance pulmonary blood flow [85]. The intention is to amplify the response of HPV in the poorly ventilated regions. Newer pharmacologic approaches to treating coronary artery disease and chronic heart failure including those with chronic pulmonary hypertension have salient effects on the remodeling of both the heart and pulmonary vasculature. However, new findings also suggest that angiotensin II receptor blockers and angiotensin-converting enzyme inhibitors may attenuate HPV response in acute hypoxia [86, 87].

Finally, future research will need to sort out the effects of acute hypoxia from chronic hypoxemia. It is apparent that a condition of chronic hypoxemia such as can be found in chronic pulmonary disease can slowly alter the normal acute response to a drop in F_iO_2 [88]. A downregulation of the HPV mechanisms might occur in the face of chronic hypoxia such that interventions such as inhaled NO may prove less efficacious [89].

In summary, the etiology of abnormal gas exchange in the patient undergoing thoracic surgery is complex, highly variable, and ever-changing throughout the course of surgery. While certain aspects of the effect of pulmonary mechanics and control of pulmonary blood flow distribution are known, the subtle interaction between the inflammatory response to surgical trauma, mechanical ventilation (especially one-lung ventilation), and the poorly understood impact of both acute and chronic pharmacologic interventions have yet to be satisfactorily defined. Until more is known, it will be extremely difficult to predict with any certainty the consequences of our anesthetic management.

References

1. Hudgel DW, Hendricks C. Palate and hypopharynx – sites of inspiratory narrowing of the upper airway during sleep. *Am Rev Respir Dis.* 1988;138:1542–7.
2. Wheatley JR, Kelly WT, Tully A, Engel LA. Pressure-diameter relationships of the upper airway in awake supine subjects. *J Appl Physiol.* 1991;70(5):2242–51.
3. Spann RW, Hyatt RE. Factors affecting upper airway resistance in conscious man. *J Appl Physiol.* 1971;31(5):708–12.
4. Bartlett D. Respiratory function of the larynx. *Physiol Rev.* 1989;69:33–57.
5. Gal TJ. Anatomy and physiology of the respiratory system and the pulmonary circulation. In: Kaplan JA, Slinger PD, editors. *Thoracic anesthesia.* 3rd ed. Philadelphia, PA: Churchill Livingstone; 2003. p. 57–70.
6. Voynow JA, Rubin BK. Mucins, mucus, and sputum. *Chest.* 2009;135:505–12.

7. Foster WM, Langenback E, Bergofsky EH. Measurement of tracheal and bronchial mucus velocities in man: relation to clearance. *J Appl Physiol.* 1980;48(6):965–71.
8. Gonda I. Particle deposition in the human respiratory tract. In: Crystal RG, West JB, Weibel ER, Barnes PJ, editors. *The lung: scientific foundations.* 2nd ed. Philadelphia, PA: Lipincott-Raven; 1997. p. 2289–308.
9. Gibson GJ, Pride NB, Empey DW. The role of inspiratory dynamic compression in upper airway obstruction. *Am Rev Respir Dis.* 1973;108:1352–60.
10. Vincken WG, Gauthier SG, Dollfuss RE, Hanson RE, Darauay CM, Cosio MG. Involvement of upper-airway muscles in extrapyramidal disorders. *N Engl J Med.* 1984;311:438–42.
11. Phipps PR, Gonda I, Bailey DC, Borham P, Bautovich G, Anderson SD. Comparison of planar and tomographic gamma scintigraphy to measure the penetrating index of inhaled aerosols. *Am Rev Respir Dis.* 1989;139:1516–23.
12. Crapo JD, Harmsen AG, Sherman MP, et al. Pulmonary immunobiology and inflammation in pulmonary diseases. *Am J Respir Crit Care Med.* 2000;162:1983–6.
13. Johnston RB. Monocytes and macrophages. *N Engl J Med.* 1988;318:747–52.
14. Bienenstock J. Bronchus-associated lymphoid tissue. *Int Arch Allergy Appl Immunol.* 1985;76:62–9.
15. Richardson JB, Ferguson CC. Neuromuscular structure and function in the airways. *Fed Proc.* 1979;38:292–308.
16. Guyenet PG. The 2008 Carl Ludwig Lecture: retrotrapezoid nucleus, CO_2 homeostasis, and breathing automaticity. *J Appl Physiol.* 2008;105:404–16.
17. Barnes PJ. Neural control of airway smooth muscle. Chapter 91. In: Crystal RG, West JB, Barnes PJ, Weibel ER, editors. *The lung: scientific foundations.* 2nd ed. Philadelphia, PA: Lippincott-Raven; 1997. p. 1269–85.
18. Caulfield MP. Muscarinic receptors, characterization, coupling and function. *Pharmacol Ther.* 1993;58:319–79.
19. Barnes PJ. Modulation of neurotransmission in airways. *Physiol Rev.* 1992;72:699–729.
20. McKenzie DK, Gandevia SC. Skeletal muscle properties: diaphragm and chest wall. In: Crystal RG, West JB, Weibel ER, Barnes PJ, editors. *The lung: scientific foundations.* 2nd ed. Philadelphia, PA: Lipincott-Raven; 1997. p. 981–91.
21. Levine S, Kaiser L, Leferovich J, et al. Cellular adaptations in the diaphragm in chronic obstructive pulmonary disease. *N Engl J Med.* 1997;337:1799–806.
22. Leith DE, Mead J. Mechanisms determining residual volume of the lungs in normal subjects. *J Appl Physiol.* 1967;23: 221–7.
23. Colin AA, Wohl MEB, Mead J, et al. Transition from dynamically maintained to relaxed end-expiratory volume in human infants. *J Appl Physiol.* 1989;67:2107–11.
24. Milic-Emili J, Henderson JAM, Dolovich MB, et al. Regional distribution of inspired gas in the lung. *J Appl Physiol.* 1966;21:749–59.
25. West JB, Dollery CT. Distribution of blood flow and ventilation-perfusion ratio in the lung, measured with radioactive carbon dioxide. *J Appl Physiol.* 1960;15:405–10.
26. Bake B, Wood L, Murphy B, et al. Effect of inspiratory flow rate on regional distribution of inspired gas. *J Appl Physiol.* 1974;37:8–17.
27. Widdicombe J. Anatomy and physiology of the airway circulation. *Am Rev Respir Dis.* 1992;146:S3–7.
28. Galvin I, Drummond GB, Nirmalan M. Distribution of blood flow and ventilation in the lung: gravity is not the only factor. *Br J Anaesth.* 2007;98:420–8.
29. Hughes M, West JB. Point: Gravity is the major factor determining the distribution of blood flow in the human lung. *J Appl Physiol.* 2008;104:1531–3.
30. Glenny RW. Counterpoint: Gravity is not the major factor determining the distribution of blood flow in the healthy human lung. *J Appl Physiol.* 2008;104:1533–5.
31. Glenny RW, Bernard S, Robertson HT. Gravity is an important but secondary determinant of regional pulmonary blood flow in upright primates. *J Appl Physiol.* 1999;86:623–32.
32. Robertson HT, Hlastala MP. Microsphere maps of regional blood flow and regional ventilation. *J Appl Physiol.* 2007;102: 1265–72.
33. Prisk GK, Guy HJB, Elliott AR, et al. Inhomogeneity of pulmonary perfusion during sustained microgravity on SLS-1. *J Appl Physiol.* 1994;76:1730–8.
34. Prisk GK, Guy HJB, Elliott AR, et al. Ventilatory inhomogeneity determined from multiple-breath washouts during sustained microgravity on Spacelab SLS-1. *J Appl Physiol.* 1995;78: 597–607.
35. Glenny RW, Lamm WJ, Bernard SL, et al. Selected contribution: redistribution of pulmonary perfusion during weightlessness and increased gravity. *J Appl Physiol.* 2000;89:1239–48.
36. Weibel ER. Fractal geometry: a design principle for living organisms. *Am J Physiol Lung Cell Mol Physiol.* 1991;261: L361–9.
37. Glenny RW. Blood flow distribution in the lung. *Chest.* 1998;114:8S–16.
38. Altemeier WA, McKinney S, Glenny RW. Fractal nature of regional ventilation distribution. *J Appl Physiol.* 2000;88:1551–7.
39. Hughes JMB, Glazier JB, Maloney JE, et al. Effect of lung volume on the distribution of pulmonary blood flow in man. *Respir Physiol.* 1968;4:58–72.
40. West JB. Regional differences in gas exchange in the lung of erect man. *J Appl Physiol.* 1962;17:893–8.
41. Wagner PD, Dantzker DR, Dueck R, et al. Ventilation-perfusion inequality in chronic obstructive pulmonary disease. *J Clin Invest.* 1977;59:203–6.
42. Bradford J, Dean H. The pulmonary circulation. *J Physiol.* 1894;16:34–96.
43. Von Euler U, Liljestrand G. Observations on the pulmonary arterial pressure in the cat. *Acta Physiol Scand.* 1946;12:301–20.
44. Duke HN. Pulmonary vasmotor responses of isolated perfused cat lungs to anoxia and hypercapnia. *Q J Exp Physiol.* 1951;36:75–88.
45. Bergofsky EH, Haas F, Porcelli R. Determination of the sensitive vascular sites from which hypoxia and hypercapnia elicit rises in pulmonary arterial pressure. *Fed Proc.* 1968;27:1420–5.
46. Domino KB, Wetstein L, Glasser SA, et al. Influence of mixed venous oxygen tension (PvO_2) on blood flow to atelectatic lung. *Anesthesiology.* 1983;59:428–34.
47. Marshall C, Marshall BE. Influence of perfuse PO_2 on hypoxic pulmonary vasoconstriction in rats. *Circ Res.* 1983;52:691–6.
48. Marshall BE, Marshall C, Benumof J, et al. Hypoxic pulmonary vasoconstriction in dogs: effects of lung segment size and oxygen tension. *J Appl Physiol.* 1981;51:1543–51.
49. Naeije R, Lejeune P, Leeman M, et al. Pulmonary vascular responses to surgical chemodenervation and chemical sympathectomy in dogs. *J Appl Physiol.* 1989;66:42–50.

50. Lejeune P, Vachiaery JL, Leeman M, et al. Absence of parasympathetic control of pulmonary vascular pressure-flow plots in hyperoxic and hypoxic dogs. *Respir Physiol*. 1989;78:123–33.
51. Robins ED, Theodore J, Burke CM, et al. Hypoxic vasoconstriction persists in the human transplanted lung. *Clin Sci*. 1987;72:283–7.
52. Aaronson PI, Robertson TP, Knock GA, et al. Hypoxic pulmonary vasoconstriction: mechanisms and controversies. *J Physiol*. 2006;570:53–8.
53. Sommer N, Dietrich A, Schermuly RT, et al. Regulation of hypoxic pulmonary vasoconstriction: basic mechanisms. *Eur Respir J*. 2008;32:1639–51.
54. Waypa GB, Chandel NS, Schumacker PT. Model for hypoxic pulmonary vasoconstriction involving mitochondrial oxygen sensing. *Circ Res*. 2001;88:1259–66.
55. Evans AM, Dipp M. Hypoxic pulmonary vasoconstriction: cyclic adenosine diphosphate-ribose, smooth muscle Ca²⁺ stores and the endothelium. *Respir Physiol Neurobiol*. 2002;132:3–15.
56. Yamamoto Y, Nakano H, Ide H, et al. Role of airway nitric oxide on the regulation of pulmonary circulation by carbon dioxide. *J Appl Physiol*. 2001;91:1121–30.
57. Talbot NP, Balanos GM, Dorrington KL, et al. Two temporal components within the human pulmonary vascular response to 2 h of isocapnic hypoxia. *J Appl Physiol*. 2005;98:1125–39.
58. Weissmann N, Zeller S, Schafer RU, et al. Impact of mitochondria and NADPH oxidases on acute and sustained hypoxic pulmonary vasoconstriction. *Am J Respir Cell Mol Biol*. 2006;34:505–13.
59. Nunn JF. Factors influencing the arterial oxygen tension during halothane anaesthesia with spontaneous respiration. *Br J Anaesth*. 1964;36:327–41.
60. Brismar B, Hedenstierna G, Lundquist H, et al. Pulmonary densities during anaesthesia with muscular relaxation – a proposal of atelectasis. *Anesthesiology*. 1985;62:422–8.
61. Lundquist H, Hedenstierna G, Strandberg A, et al. CT-assessment of dependent lung densities in man during general anaesthesia. *Acta Radiol*. 1995;36:626–32.
62. Reber A, Bein T, Hogman M, et al. Lung aeration and pulmonary gas exchange during lumbar epidural anaesthesia and in the lithotomy position in elderly patients. *Anaesthesia*. 1998;53:854–61.
63. Tenling A, Joachimsson PO, Tyden H, et al. Thoracic epidural anaesthesia as an adjunct to general anaesthesia for cardiac surgery: effects on ventilation-perfusion relationships. *Anesthesiology*. 1987;66:157–67.
64. Magnusson L, Spahn DR. New concepts of atelectasis during general anaesthesia. *Br J Anaesth*. 2003;91:61–72.
65. Froese AB, Bryan AC. Effects of anaesthesia and paralysis on diaphragmatic mechanics in man. *Anesthesiology*. 1974;41:242–55.
66. Warner DO, Warner MA, Ritman EL. Atelectasis and chest wall shape during halothane anaesthesia. *Anesthesiology*. 1996;85:49–59.
67. Reber A, Nylund U, Hedenstierna G. Position and shape of the diaphragm: implications for atelectasis formation. *Anaesthesia*. 1998;53:1054–61.
68. Loring SH, Butler JP. Gas exchange in body cavities. In: Farhi LE, Tenney SM, editors. *Handbook of physiology. Section 3. The respiratory system. Volume 4, gas exchange*. Bethesda, MD: American Physiological Society; 1987. p. 283–95.
69. Joyce CJ, Baker AB, Kennedy RR. Gas uptake from an unventilated area of the lung: computer model of absorption atelectasis. *J Appl Physiol*. 1993;74:1107–16.
70. Joyce CJ, Williams AB. Kinetics of absorption atelectasis during anaesthesia: a mathematical model. *J Appl Physiol*. 1999;86:1116–25.
71. Rothen HU, Sporre B, Engberg G, et al. Influence of gas composition on recurrence of atelectasis after a re-expansion maneuver during general anaesthesia. *Anesthesiology*. 1995;82:832–42.
72. Domino KB, Borowec L, Alexander CM, et al. Influence of isoflurane on hypoxic pulmonary vasoconstriction in dogs. *Anesthesiology*. 1986;64:423–9.
73. Abe K, Mashimo T, Yoshiya I. Arterial oxygenation and shunt fraction during one-lung ventilation: a comparison of isoflurane and sevoflurane. *Anesth Analg*. 1998;86:1266–70.
74. Pagel PS, Fu JL, Damask MC, et al. Desflurane and isoflurane produce similar alterations in systemic and pulmonary hemodynamics and arterial oxygenation in patients undergoing one-lung ventilation during thoracotomy. *Anesth Analg*. 1998;87:800–7.
75. Schwarzkopf K, Schreiber T, Preussler N-P, et al. Lung perfusion, shunt fraction, and oxygenation during one-lung ventilation in pigs: the effects of desflurane, isoflurane, and propofol. *J Cardiothorac Vasc Anesth*. 2003;17:73–5.
76. Benumof JL, Wahrenbrock EA. Local effects of anaesthetics on regional hypoxic pulmonary vasoconstriction. *Anesthesiology*. 1975;43:525–32.
77. Reid CW, Slinger PD, Lenis S. A comparison of the effects of propofol-alfentanil versus isoflurane anaesthesia on arterial oxygenation during one-lung ventilation. *J Cardiothorac Vasc Anesth*. 1996;10:860–3.
78. Beck DH, Doepfner UR, Sinemus C, et al. Effects of sevoflurane and propofol on pulmonary shunt fraction during one-lung ventilation for thoracic surgery. *Br J Anaesth*. 2001;86:38–43.
79. Ishibe Y, Shiokawa Y, Umeda T, et al. The effect of thoracic epidural anaesthesia on hypoxic pulmonary vasoconstriction in dogs: an analysis of the pressure-flow curve. *Anesth Analg*. 1996;82:1049–55.
80. Parsons GH, Leventhal JP, Hansen MM, et al. Effect of sodium nitroprusside on hypoxic vasoconstriction in the dog. *J Appl Physiol*. 1981;51:288–92.
81. Casthely PA, Lear S, Cottrell JE, et al. Intrapulmonary shunting during induced hypotension. *Anesth Analg*. 1982;61:231–5.
82. Kato R, Sato J, Hishino T. Milrinone decreases both pulmonary arterial and venous resistances in the hypoxic dog. *Br J Anaesth*. 1998;81:920–4.
83. Weissmann N, Gerigk B, Kocer O, et al. Hypoxia-induced pulmonary hypertension: different impact of iloprost, sildenafil, and nitric oxide. *Respir Med*. 2007;101:2125–32.
84. Reichenberger F, Kohstall MG, Seeger T, et al. Effect of sildenafil on hypoxia-induced changes in pulmonary circulation and right ventricular function. *Respir Physiol Neurobiol*. 2007;159:196–201.
85. Fesler P, Pagnamenta A, Rondelet B, et al. Effects of sildenafil on hypoxic pulmonary vascular function in dogs. *J Appl Physiol*. 2006;101:1085–90.
86. Kiely DG, Cargill RI, Lipworth BJ. Angiotensin II receptor blockade and effects on pulmonary hemodynamics and hypoxic pulmonary vasoconstriction in humans. *Chest*. 1996;110:698–703.
87. Cargill RI, Lipworth BJ. Lisinopril attenuates acute hypoxic pulmonary vasoconstriction in humans. *Chest*. 1996;109:424–9.
88. McMurry IF, Petrun MD, Reeves JT. Lungs from chronically hypoxic rats have decreased pressor response to acute hypoxia. *Am J Physiol*. 1978;235:H104–9.
89. Weissmann N, Nollen M, Gerigk B, et al. Down-regulation of hypoxic vasoconstriction by chronic hypoxia in rabbits: effects of nitric oxide. *Am J Physiol*. 2003;284:H931–8.
90. Wagner PD, Laravuso B, Goldzimber E, et al. Distributions of ventilation-perfusion ratios in dogs with normal and abnormal lungs. *J Appl Physiol*. 1975;38:1099–109.

5

Physiology of the Lateral Decubitus Position, Open Chest and One-Lung Ventilation

Jens Lohser and Seiji Ishikawa

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Key Points

- Ventilation and perfusion matching is optimized for gas exchange.
- Induction of anesthesia, one-lung ventilation (OLV) and opening of the chest progressively uncouple ventilation–perfusion (V/Q) matching.
- Hypoxic pulmonary vasoconstriction (HPV) improves V/Q matching during OLV, but can be impaired by anesthetic interventions.

Introduction

Early attempts at intrathoracic surgery in nonventilated patients were fraught with rapidly developing respiratory distress and a fast moving operative field. The difficulty with performing a thoracotomy in a spontaneously breathing patient, for both the patient and the surgeon, is easily explained by two phenomena: *Pendel-luft* and *Mediastinal shift* (Fig. 5.1) [1]. Both phenomena can be explained by the fact that the pleural interface has been disrupted in the open hemithorax so that no negative intrathoracic pressure is being created in response to a spontaneous inspiratory effort and chest-wall expansion. In the closed hemithorax, on the other hand, chest-wall expansion and the resulting negative intrathoracic pressure will produce gas flow into the lung via the mainstem bronchus. However, inspiratory gas flow will not only come from the trachea, but also from the operative lung, which is free to collapse due

to the surgical pneumothorax. Inspiration therefore results in nonoperative lung expansion and operative lung retraction. The reverse process occurs during expiration, where bulk expiratory gas flow, from the nonoperative lung, not only escapes via the mainstem bronchus into the trachea, but also back into the re-expanding operative lung. This process results in the “pendular” motion of the lung with inspiration and expiration. Mediastinal shift occurs due to a similar process. The negative inspiratory pressure in the closed hemithorax is equally applied to the mediastinum, which is secondarily pulled away from the open thorax during inspiration. The reverse is true during expiration, where positive intrathoracic pressure pushes the mediastinum across into the open thorax. When combined, these two mechanisms explain the difficult exposure for the operating surgeon due to a fast moving operating field, and the rapidly developing respiratory distress in the patient secondary to inefficient to-and-fro ventilation with limited CO_2 elimination and fresh gas entrainment (Fig. 5.1). Interestingly, awake thoracic surgery is being re-popularized in certain high-risk individuals, but the use of video-assisted thoracoscopic surgery (VATS), which avoids opening of the hemithorax, minimizes the above stated issues [3].

Selective ventilation of one lung was first described in 1931 and quickly resulted in increasingly complex lung resection surgery [4]. While infinitely better tolerated than spontaneous respiration, hypoxia was a frequent occurrence during the early years of OLV. Extensive research over the ensuing decades has clarified the basic physiology governing pulmonary perfusion (Q) and ventilation (V), as well as the disturbances that are

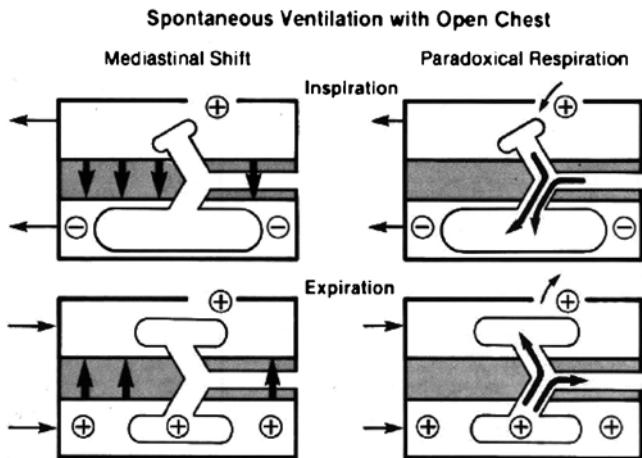


FIG. 5.1. Schematic representation of “Pendel-luft” and mediastinal shift. See text for details (modified from Benumof [2]. © Elsevier 1995).

caused by anesthetic and surgical interventions. Knowledge of the basic physiology is necessary to appreciate ventilation/perfusion (V/Q) disturbances during OLV.

Perfusion

Pulmonary blood flow is essential for multiple processes. Pulmonary arterial blood carries carbon dioxide to the alveoli for removal and exhalation. Pulmonary venous blood provides filling and oxygen to the left heart to support systemic perfusion and metabolic oxygen demand, respectively. Because of the closed nature of the circulatory system, the entire cardiac output (CO) has to pass through the pulmonary circulation. Pulmonary perfusion pressures are significantly lower than systemic perfusion pressures and become further reduced by 1-cm H_2O for each centimeter of elevation that blood flow has to travel above the level of the heart. Perfusion is therefore not uniform across the lung, as pulmonary arterial (P_{pa}) and venous (P_{pv}) pressures are dependent on the relative elevation above the heart, whereas the extrinsic compressive force of the alveolar distending pressure (P_A) is relatively constant. The interplay of pressures across the lung results in distinct territories of lung perfusion, which are known as the West Zones (Fig. 5.2a) [7, 8]. Zone 1 exists in the most superior aspect of the lung and is characterized by alveolar pressures that exceed intravascular pressures ($P_A > P_{pa} > P_{pv}$). This results in capillary collapse and secondary complete obstruction of blood flow. Zone 1 therefore represents alveolar “dead space.” While Zone 1 is minimal under normal circumstances, it may increase in the presence of increased P_A (positive pressure ventilation) or decreased P_{pa} (decreased CO). Moving inferiorly in the lung, P_{pa} values increase due to the lesser elevation above the heart and begin to exceed P_A . This characterizes Zone 2 ($P_{pa} > P_A > P_{pv}$) where P_{pa} exceeds P_A resulting in capillary blood flow. As P_A continues to exceed P_{pv} ,

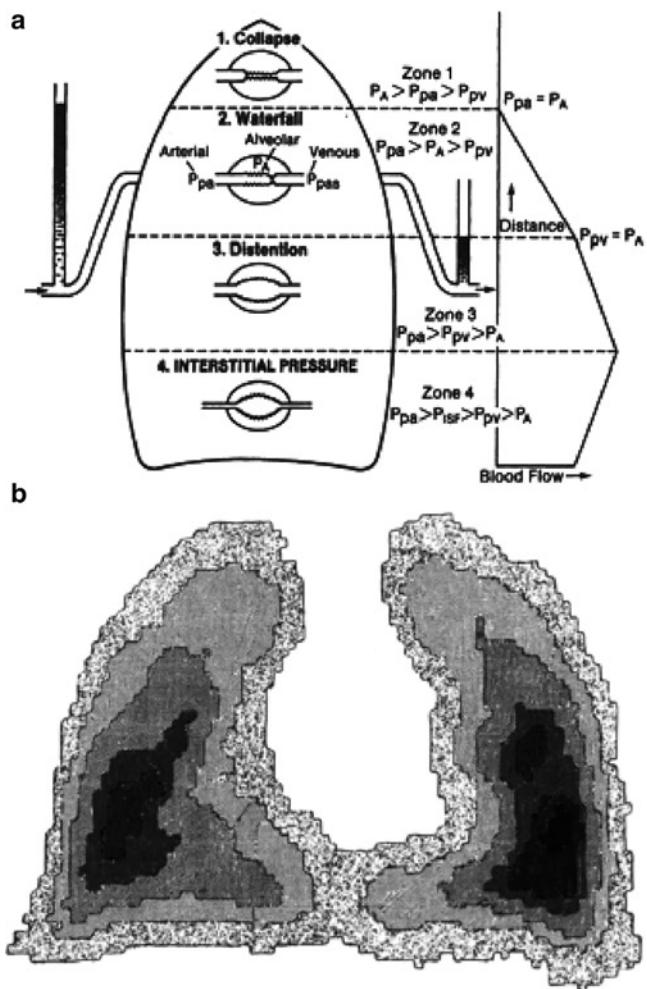


FIG. 5.2. (a, b) Pulmonary blood flow distribution as it relates to the alveolar pressure (P_A), the pulmonary arterial pressure (P_{pa}), the pulmonary venous pressure (P_{pv}) and the interstitial pressure (P_{is}) at various gravitational levels. Classic West Zones of blood flow distribution in the upright position (a). In vivo perfusion scanning illustrating central-to-peripheral, in addition to gravitational blood flow distribution, in the upright position (b). See text for further details ((a) modified from West [5] and (b) Hakim et al. [6], with permission).

capillary blood flow remains dependent on the differential between P_{pa} and P_A . This relationship has been likened to a waterfall, as the amount of flow is dependent on the upstream “water” pressure (P_{pa}), relative to the level of the mountain ledge or dam (P_A), but independent of the downstream “water” level (P_{pv}). Zone 3 ($P_{pa} > P_{pv} > P_A$) is reached when P_{pv} begins to exceed P_A , resulting in pulmonary perfusion independent of P_A and only determined by difference between P_{pa} and P_{pv} . Zone 4 ($P_{pa} > P_{is} > P_{pv} > P_A$) is that portion of the lung where interstitial pressure P_{is} is higher than venous pressure P_{pv} , resulting in a reduction in blood flow relative to the pressure differential between P_{pa} and P_{is} . This is analogous to the patient with increased intracranial pressure (ICP) due to cerebral edema, where the “interstitial” pressure (ICP) exceeds the venous outflow pressure (CVP) and therefore reduces

the cerebral perfusion pressure. Zone 4 can exist in the most inferior portions of the lung, or may alternatively be created by exhalation to low lung volumes or increased interstitial pressures such as in volume-overload [8]. One should keep in mind that the West zones are an oversimplified static picture of a dynamic, cyclical system, as lung regions may move through various zones depending on the stage of the cardiac and respiratory cycle that they are in. For example, a given zone 2 lung region may become zone 1 during diastole (low P_{pa}) and positive pressure inspiration (high P_A) or may become zone 3 in systole (high P_{pa}) and mechanical expiration (low P_A). The gravitational model of the West zones helps to illustrate the basis of V/Q mismatch in the lungs, but only partially reflects human physiology. *In vivo* perfusion scanning, with tagged albumin micro-aggregates in healthy volunteers, has demonstrated a combination of gravitational distribution and an “onion-like” layering, with reduced flow at the periphery of the lung and higher flow toward the hilum (Fig. 5.2b) [6]. It has also been shown that the perfusion of the left lung, in the dependent left lateral decubitus position, is lower than would be expected based simply on gravity redistribution. Compression and/or distortion elicited by the heart and mediastinum is the likely cause for this reduction [9].

The pulmonary vascular bed is a low-resistance conduit and possesses significant recruitable territory, which helps to offset any increases in pressure. Mild increases in P_{pa} cause progressive recruitment of previously nonperfused vasculature. Once recruitment is complete, further increases in P_{pa} distend the pulmonary vessels, which accommodates increases in blood flow and helps to minimize increases in right ventricular afterload. These modifications allow pulmonary pressures to stay low, even when CO is increased to levels as high as 30 L/min during exercise [10]. At extreme levels of P_{pa} , distention of blood vessels will fail to decrease intravascular pressures resulting in transudation of fluid into the interstitium [11]. Vascular resistance within the pulmonary circulation is also influenced by the degree of lung inflation. There are two populations of pulmonary vessels that exhibit opposing responses to lung inflation. Alveolar capillaries are exposed to intra-alveolar pressures and therefore experience increasing resistance to flow, or may actually collapse, as lung volumes increase. Intraparenchymal, extra-alveolar vessels, on the other hand, experience outward radial traction with lung expansion, which progressively decreases their resistance. The cumulative effect is a parabolic resistance curve, with minimal pulmonary vascular resistance (PVR) at functional residual capacity (FRC) and progressive increases in resistance at extremes of lung volume (Fig. 4.5).

HPV

Oxygen-sensing mechanisms are active throughout the human body (placenta, ductus arteriosus, carotid body and pulmonary arteries) and have been reviewed in detail [12]. HPV of the pulmonary arterial bed is one such mechanism. In the fetus HPV-induced high PVR results in diversion of blood flow across the

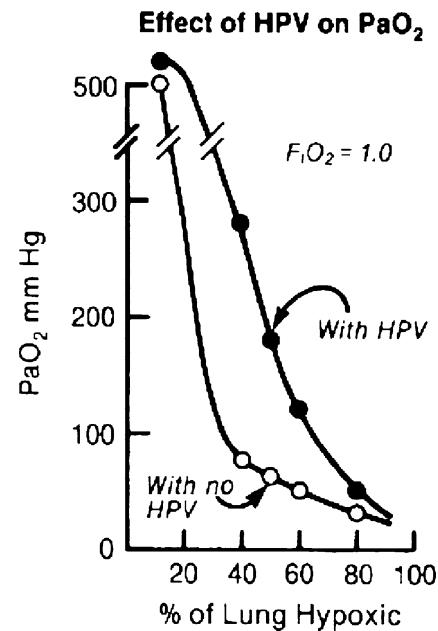


FIG. 5.3. Model of the effect of hypoxic pulmonary vasoconstriction (HPV) on P_aO_2 as a function of the percent of lung that is hypoxic. The model assumes an F_1O_2 of 1.0, normal hemoglobin, cardiac output and oxygen consumption. The HPV benefit is maximal when 30–70% of the lung are hypoxic (modified from Benumof [2]. © Elsevier 1995).

foramen ovale and ductus arteriosus. HPV remains important ex utero, as it allows V/Q matching by reducing perfusion to poorly oxygenated lung tissue. HPV is active in the physiologic range (P_AO_2 40–100 mmHg in the adult) and proportional to not only the severity of the hypoxia, but also the amount of hypoxic lung. HPV is maximal if between 30 and 70% of the lung are hypoxic (Fig. 5.3). Low partial pressure of oxygen results in inhibition of potassium currents, which leads to membrane depolarization and calcium entry through L-type calcium channels. Extracellular calcium entry, plus calcium release from the sarcoplasmic reticulum, culminates in smooth muscle contraction, primarily in low-resistance pulmonary arteries with a diameter less than 500 μ m [12]. The primary stimulus for HPV appears to be the alveolar partial pressure of oxygen (P_AO_2); however, the pulmonary venous partial pressure of oxygen (P_vO_2) is also involved. HPV is maximal at normal P_vO_2 levels, but is inhibited at high or low levels. Low P_vO_2 , for example in low CO states, results in a decrease in P_aO_2 and therefore generalized, competing vasoconstriction. Conversely, high P_vO_2 in the setting of sepsis will decrease the vasoconstrictor response in hypoxic areas due to the generalized increase in P_aO_2 . Vasoconstriction occurs in a biphasic temporal fashion. The early response occurs within seconds and reaches an initial plateau at 15 min, followed by a late response resulting in maximal vasoconstriction at 4 h [13–16]. HPV reduces the shunt flow through the operative lung by roughly 40%, facilitating the safe conduct of OLV (Fig. 5.4), although some have questioned its true clinical importance [17].

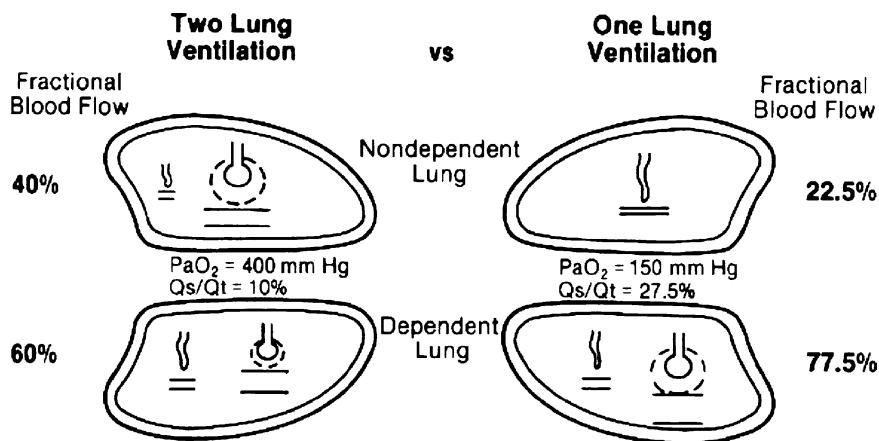


FIG. 5.4. Schematic representation of two- vs. one-lung ventilation. Typical values for fractional blood flow to the nondependent and dependent lungs as well as P_{aO_2} and Qs/Qt for the two scenarios are shown. The Qs/Qt during two-lung ventilation is assumed to be distributed equally between the two lungs (5% each). The main difference between two- and one-lung ventilation is the obligatory shunt through the nonventilated lung. HPV is able to reduce the shunt flow through the nondependent lung by 50%. Total shunt fraction in the one-lung ventilation setting consists of the residual shunt flow through the nondependent lung plus the baseline 5% shunt through the dependent lung (modified from Benumof [2]. © Elsevier 1995).

Extremes of HPV may cause harm. Over-activity, particularly during exercise at high altitudes, may result in high-altitude pulmonary edema [14]. The opposite is true in thoracic anesthesia where inhibition of HPV may result in intra-operative hypoxemia. Many studies have attempted to identify agents or interventions that potentiate or inhibit the pulmonary vasoconstrictor response to hypoxia. Most research has been performed on animals, as interventions are more easily standardized. Perioperative HPV modifiers are summarized in Table 5.1.

Anesthetic Modifiers

Inhibition of HPV by inhalational anesthesia has long been recognized. Ether, halothane and nitrous oxide inhibit HPV in a dose-dependent fashion, and the underlying intracellular mechanisms have been described for halothane [64]. The effect of the newer inhalation anesthetics such as isoflurane, desflurane and sevoflurane is less certain. They appear to be neutral toward HPV, or at least not cause significant depression in clinically relevant doses. Intravenous anesthesia with propofol has been proposed as a means of avoiding HPV modulation, but the improvement in oxygenation is clinically insignificant, except in marginal patients. Results on the influence of thoracic epidural anesthesia (TEA) on oxygenation have been conflicting. Garutti et al. showed an increase in pulmonary venous admixture and secondary worse oxygenation, which may have been due to a drop in CO [65]. Multiple other studies failed to demonstrate an effect of TEA on oxygenation during OLV, when hemodynamic variables were maintained [34–36]. Traditional thoracic teaching has emphasized to keep patients warm and dry, which is supported by the fact that hypothermia and both, hemodilution and increased left atrial pressure, inhibit HPV. Almitrine and nitric oxide (NO) have been shown to provide a potential avenue for HPV modulation. Almitrine, a respiratory stimulant that causes pulmonary

TABLE 5.1. Peri-operative modifiers of hypoxic pulmonary vasoconstriction.

	Effect	References
Patient factors		
COPD	–	[18]
Cirrhosis	–	[19]
Sepsis	–	[20] ^a
Pregnancy	–	[21] ^a
Female sex	–	[22] ^a
Exercise	–	[23] ^a
Systemic HTN	+	[24]
EtOH	+	[25] ^a
Physiologic changes		
Metabolic acidosis	+	[26] ^a
Respiratory acidosis	0	[26] ^a
Metabolic alkalosis	–	[26] ^a
Respiratory alkalosis	–	[26] ^a
Hypercapnia	+	[13]
Hypocapnia	–	[13]
Hyperthermia	+	[27] ^a
Hypothermia	–	[27] ^a
Increased LAP	–	[28] ^a
Increased P_vO_2	–	[29] ^a
Decreased P_vO_2	+	[29] ^a
Peri-operative interventions		
Trendelenburg	–	[30]
Lateral decubitus	+	[31]
Supine position	0	[31]
Surgical lung retraction	+	[32]
Hemodilution	–	[33]
Epidural anesthesia	0	[34–37]
Inhaled NO	0	[37]
Pharmacologic agents		
<i>Inhalational anesthetics</i>		
Nitrous oxide	–	[38]
Halothane	–	[39]
Enflurane	0	[40]
Isoflurane	0/–	[41]
Desflurane	0	[42]
Sevoflurane	0	[43]

(continued)

TABLE 5.1. (continued)

	Effect	References
<i>Intravenous anesthetics</i>		
Propofol	0/+	[43, 44] ^a
Ketamine	0	[44] ^a
Opioids	0	[45] ^a
<i>Calcium channel blockers</i>		
Verapamil	–	[39]
Diltiazem	0	[46]
<i>Adrenergic blockers</i>		
Propranolol	+	[47] ^a
Phenoxybenzamine	–	[47] ^a
Phentolamine	–	[48]
Clonidine	+	[49] ^a
<i>Vasodilators</i>		
Hydralazine	–	[48]
Nitroglycerin	–	[50] ^a
Nitroprusside	–	[51]
Sildenafil	0	[52]
<i>Vasoactive agents</i>		
Dopamine	?	[53] ^a
Isoproterenol	–	[54] ^a
Norepinephrine	–	[54] ^a
Phenylephrine	+	[55]
Vasopressin	0?	[56] ^a
<i>Other</i>		
Losartan (ARB)	–	[57]
Lisinopril (ACE-I)	–	[58]
Methylprednisolone	0	[59]
Indomethacin	+	[50] ^a
ASA	+	[50] ^a
Prostacyclin	–	[60]
PGE ₁	–	[61] ^a
Salbutamol	+	[62]
Atrovent	+	[62]
Lidocaine	+	[38] ^a

^aAnimal data

Modified from Lohser [63], with permission

vasoconstriction when given intravenously, has been shown to potentiate HPV and improve oxygenation. Endogenous NO causes vasodilation and thereby inhibits HPV; however if given by the inhalational route to the ventilated lung during OLV, NO causes localized vasodilation and thereby decreases shunt fraction. The combination of intravenous almitrine with inhaled NO results in synergistic improvement in *V/Q* matching and oxygenation. Almitrine, however, is not widely available and is associated with the potential for significant toxicity. Although clearly efficacious, the focus on HPV manipulation with potentially dangerous agents such as almitrine has been called a distraction from more common reasons for desaturation, such as hypoventilation of the dependent lung [17].

Other Modifiers of HPV

Surgical retraction can assist HPV by increasing PVR in the operative lung [32]; however, the release of vasoactive substances secondary to the manipulation may conversely result in an inhibition of HPV [66]. Ligation of pulmonary

vessels during lung resection results in the permanent exclusion of vascular territory and thereby a reduction in shunt flow [66]. The side of surgery influences the extent of shunt flow, as the larger right lung receives a 10% higher proportion of CO than the left lung. Positioning is important as the lateral decubitus position allows for a gravity-induced reduction in shunt flow to the nondependent lung. Procedures that call for supine positioning, on the other hand, are hampered by higher shunt flow to the nondependent lung and may have higher rates of intra-operative desaturations [31]. Similarly, addition of a head-down tilt to the left lateral position has been shown to worsen oxygenation during OLV, likely due to dependent lung compression by abdominal contents [30].

Cardiac Output and Arterial Oxygenation

Arterial oxygen content (CaO₂) is influenced by end-capillary oxygen content (CcO₂), oxygen consumption (VO₂), CO (Q_t) and shunt flow (Q_s). CaO₂ can be calculated using Eq. (5.1), and the interaction of the various factors on CaO₂ is illustrated in Fig. 5.5 [67].

$$\text{CaO}_2 = \text{CcO}_2 - (\text{VO}_2 / \text{Q}_t) \times \left(\frac{\text{Q}_s / \text{Q}_t}{10 \times (1 - \text{Q}_s / \text{Q}_t)} \right) \quad (5.1)$$

The influence of CO on arterial oxygenation during OLV has been studied repeatedly. Slinger and Scott showed a direct correlation between increasing CO and improving oxygenation in patients during OLV [68]. Similarly, CO augmented by a small dose of dobutamine (5 µg/kg/min) has been shown to improve arterial oxygenation and decrease shunt fraction [69, 70]. However, larger doses of dobutamine have been shown to adversely affect arterial oxygenation in a porcine model of OLV. Russell and James increased CO to supranormal levels (two to three times normal) with dopamine, dobutamine, adrenaline or isoproterenol [71, 72]. They demonstrated that while high CO increases mixed venous oxygenation, this benefit is overridden by an increase in shunt fraction, resulting in impaired arterial oxygenation. The shunt fraction is likely increased due to weakened HPV in the face of increases in pulmonary arterial pressure [28, 73]. Animal studies have similarly shown that high doses (20–25 µg/kg/min) of dopamine and dobutamine inhibit HPV response in dogs with left lower lobe hypoxia [74] and one-lung atelectasis [53]. At low CO, oxygenation will therefore be impaired secondary to a low mixed venous oxygen saturation, despite a relatively low shunt fraction. At supranormal CO, on the other hand, oxygenation will be impaired due to an increased shunt fraction, despite the high mixed venous saturation (Fig. 5.6). This interplay bears some resemblance to the opposing effects of alveolar and parenchymal vascular resistance on PVR (Fig. 4.5). Maintenance or restoration of “normal” CO is therefore important for oxygenation during OLV. The availability of noninvasive monitoring devices makes CO data more readily available and allows for appropriate titration of inotropes when required.

FIG. 5.5. The influence of cardiac output on arterial oxygen content (CaO_2). Plot A: hemoglobin concentration 15 g/dL, oxygen consumption (VO_2) 150 mL/min, shunt fraction (Q_s/Q_t) 0.2. Plot B: hemoglobin concentration 15 g/dL, VO_2 150 mL/min, Q_s/Q_t 0.4. Plot C: hemoglobin concentration 15 g/dL, VO_2 75 mL/min, Q_s/Q_t 0.2. Plot D: hemoglobin concentration 10 g/dL, VO_2 150 mL/min, Q_s/Q_t 0.2 (from Levin et al. [67], with permission).

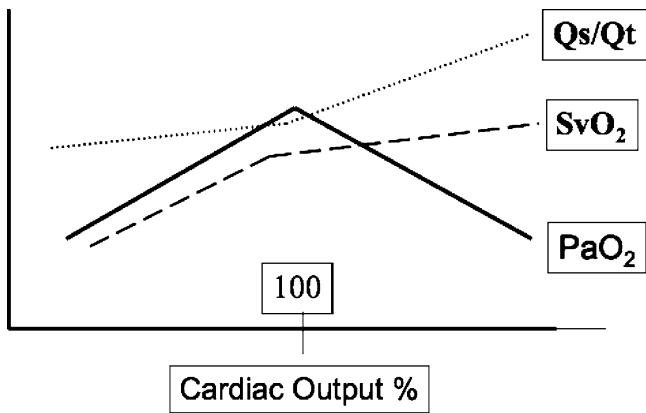
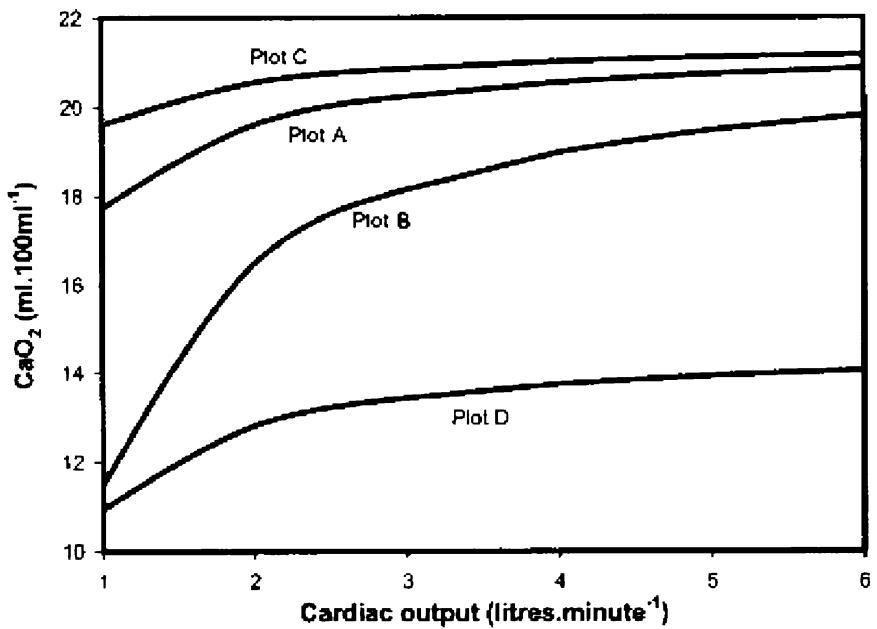


FIG. 5.6. Effect of cardiac output on P_{aO_2} during OLV (on the basis of the data from Slinger and Scott [68] and Russell and James [71]).

Ventilation

Similar to pulmonary perfusion, gravitational forces also affect the distribution of ventilation throughout the lung. The negative pressure of the visceral–parietal pleural interface forces the lung to maintain the shape of the hemithorax. Disruption of that interface (as in a pneumothorax) results in recoil deflation of the lung, which, analogous to a fluid-filled balloon, will take on a more globular shape (Fig. 5.7). The same forces are active even with an intact pleural interface and affect the cumulative transpulmonary pressure. The inherent tendency of the lung to want to collapse away from the upper chest-wall adds to the negative pleural pressure at the top of the lung, while the tendency of the dependent lung to want to

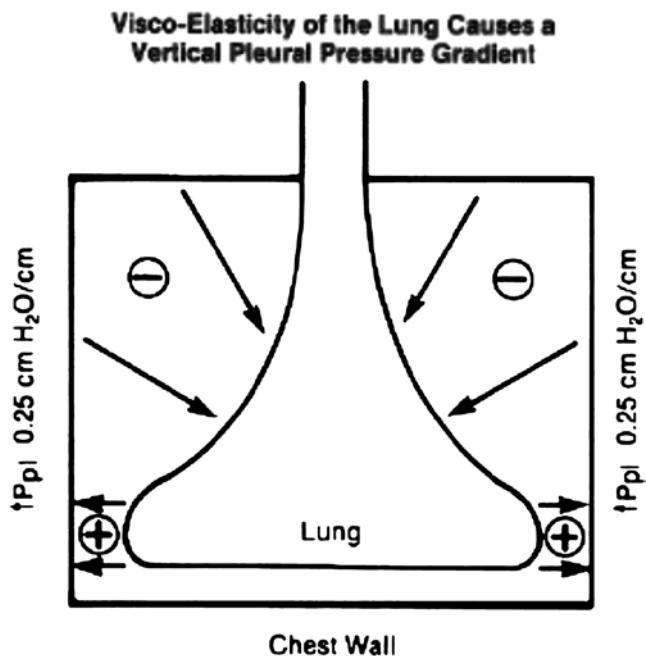


FIG. 5.7. Schematic diagram of the lung within the chest wall illustrating the tendency of the lung to assume a globular shape because of the lung's viscoelastic nature. The tendency of the top of the lung to collapse inward creates a relatively more negative pressure at the top of the lung. Thus, pleural pressure increases by 0.25 cm H_2O per centimeter of lung dependency (modified from Benumof [75]. © Elsevier 1983).

push outward reduces negative pleural pressure at the bottom of the lung. The resulting vertical pressure gradient accounts for a change of 0.25 cm H_2O per centimeter of vertical distance

along the lung. On the basis of a height of 30 cm of the upright lung this corresponds to a change in transpulmonary pressure (P_{pl}) of $30 \times 0.25 = 7.5$ cm H₂O between the top and the bottom of the lung [76]. The distending force (P_A) is the same for all alveoli; however, P_{pl} becomes less negative toward the bottom of the lung. The net effect is that the transalveolar distending pressure ($P_A - P_{pl}$) is higher at the top of the lung, resulting in a larger alveolar volume compared to the bottom of the lung. In fact, this difference in size can be as much as fourfold. While the dependent alveoli are relatively small and compressed, they fall on the steep (compliant) portion of the volume–compliance curve and receive a disproportionately larger amount of the alveolar ventilation. The larger alveoli of the upper lung fall on the flat (noncompliant) portion of the volume–compliance curve and therefore change little during tidal respiration (Fig. 4.3) [77].

Ventilation–Perfusion Matching

Efficient gas exchange hinges on matching of perfusion and ventilation. Both ventilation and perfusion increase progressively from nondependent to dependent areas, but the change in perfusion is more extreme and ranges from zero flow to high flows. As a result, nondependent areas tend to be relatively underperfused ($V/Q >> 1$), whereas the dependent areas are relatively overperfused ($V/Q << 1$) (Fig. 4.6). Postcapillary blood from the under-ventilated, dependent lung zones ($V/Q << 1$), therefore, tends to be relatively hypoxic and slightly hypercapnic. Nondependent lung zones, which are relatively over-ventilated ($V/Q >> 1$), are able to compensate by removing excess CO₂, but due to the flat O₂–hemoglobin curve, they are less capable of increasing oxygen uptake. High V/Q areas therefore compensate for carbon dioxide, but not for oxygen, exchange. As a result, the alveolar–arterial (A–a) gradient, in the setting of significant V/Q mismatch, is large for oxygen and relatively small for carbon dioxide (Fig. 5.8) [78].

OLV provides a significant challenge to V/Q matching. Once lung isolation has been established, residual oxygen is gradually absorbed from the nonventilated lung until complete absorption atelectasis has occurred. At that point, pulmonary blood flow to the operative lung is entirely wasted perfusion. The resulting right-to-left shunt through the nonventilated lung is in addition to the normal 5% of shunt in the ventilated lung. As blood flow to each lung is roughly equal (right lung 55% of CO, left lung 45% of CO), this mathematically results in a shunt fraction of at least 50%. Observed shunt fractions are fortunately much lower (Fig. 5.4). Both passive and active mechanisms decrease the blood flow through the operative lung. Surgical manipulation and, in the lateral position, gravity passively reduce the blood flow to the nonventilated lung. In addition, HPV actively increases vascular resistance in the nonventilated lung, resulting in a gradual decrease in shunt fraction.

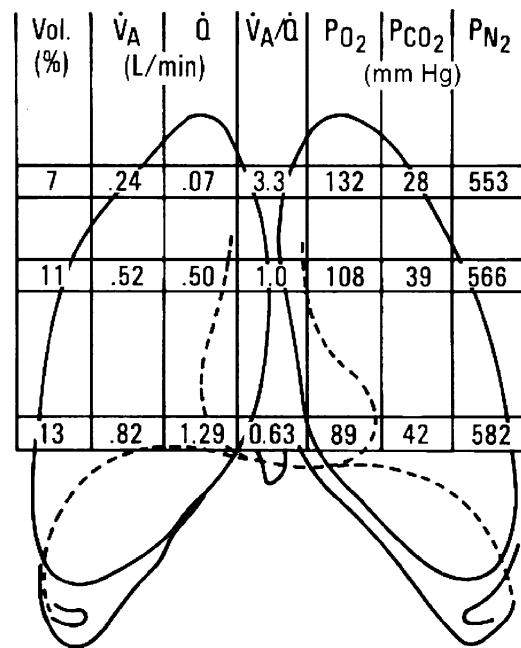


FIG. 5.8. The ventilation–perfusion ratio and the regional composition of alveolar gas. Compared with the top of the lung, the bottom has a low ventilation–perfusion ratio and is relatively hypoxic and hypercapnic (from West [78], with permission).

V/Q Matching in the Lateral Position

Awake

The distribution of alveoli on the compliance curve is maintained when an awake, spontaneously breathing patient assumes the lateral position. Dependent alveoli remain small and compliant, whereas nondependent alveoli stay large and noncompliant. Because of the position change, however, different areas of the lung are now dependent and nondependent. While caudal regions are small and compliant in the upright position, in the lateral position it is the dependent (down) lung, which receives most of the ventilation. Additionally, the cephalad displacement of the dependent diaphragm by abdominal contents results in more effective diaphragmatic muscle contraction. The net result is preferential ventilation of the dependent lung in the lateral position relative to the nondependent lung (Fig. 5.9) [2, 15].

Perfusion is similarly affected in the lateral decubitus position. The gravity dependent distribution of flow is maintained, with a roughly 10% shift of CO to the dependent lung. A dependent right lung will therefore receive 65% of CO, compared to the 55% it receives in the upright or supine position. For a dependent left lung this will result in an increase from the normal 45% of CO towards 55% of CO (Fig. 5.10) [79]. When combined, the lateral position favors the dependent lung in ventilation and perfusion, and V/Q matching is maintained similar to the upright position.

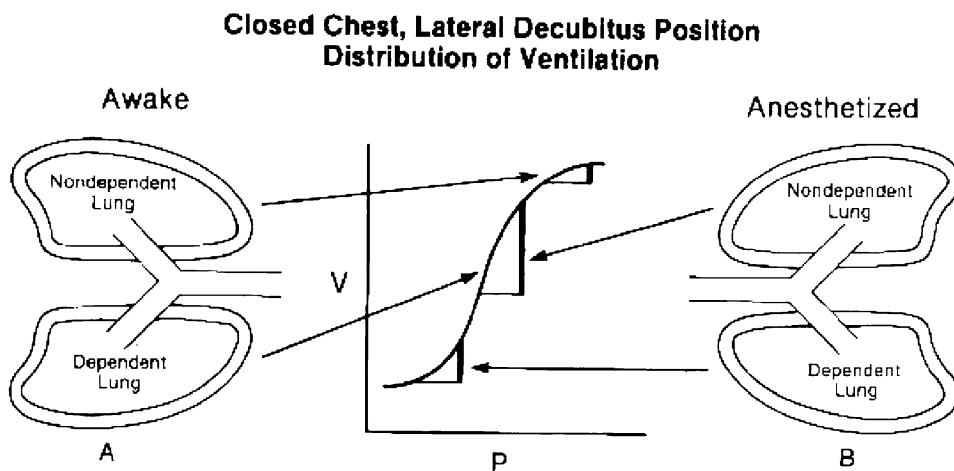


FIG. 5.9. Schematic diagram of a patient in the lateral decubitus position. The change in the distribution of ventilation with the transition from the awake state to the anesthetized state is illustrated (modified from Benumof [2]. © Elsevier 1995).

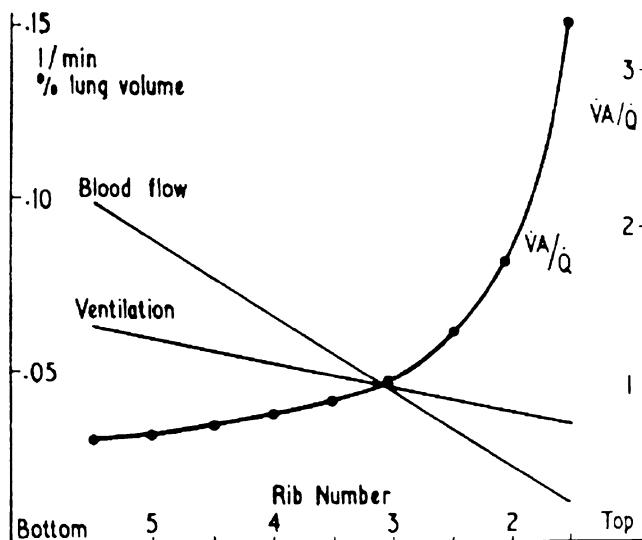


FIG. 5.10. Schematic representation of the effects of gravity on the distribution of pulmonary blood flow in the lateral decubitus position. The vertical gradient in the lateral decubitus position is less than that in the upright position (Fig. 5.2). Consequently there is less zone 1 and more zones 2 and 3 blood flow in the lateral decubitus position compared with the upright position (alveolar pressure (P_A), pulmonary arterial pressure (P_a), pulmonary venous pressure (P_v)) (modified from Benumof [2]. © Elsevier 1995).

Anesthetized

Induction of anesthesia decreases diaphragmatic and inspiratory muscle tone, which results in a 15–20% drop in FRC in both lungs. The change in lung volume alters the relative position of each lung on the compliance curve. The dependent lung drops from the steep portion of the volume–pressure curve, to the flat, noncompliant position. The nondependent lung on the other hand drops from the shallow position of the curve into the steeper portion previously occupied by the dependent lung

(Fig. 5.9). As a result, the nondependent lung is now more compliant than the dependent lung and becomes preferentially ventilated [2, 80, 81]. The distribution of perfusion, on the other hand, is not affected by the induction of anesthesia. Consequently, ventilation and perfusion have become uncoupled with the nondependent lung receiving the bulk of ventilation (but little perfusion) and the dependent lung receiving the majority of perfusion (but little ventilation) [2, 15].

Paralyzed/Ventilated

Muscle relaxation, which entirely removes diaphragmatic and inspiratory muscle tone, further alters the distribution of ventilation. Diaphragmatic contraction played a more dominant role due to the favorable, higher resting position in the lateral decubitus (Fig. 5.11). Once paralyzed, static displacement of the relaxed diaphragm by abdominal contents and the gravity force of the mediastinum further restrict the lower lung, resulting in an additional decrease in its compliance (Fig. 6.3). Coupled with the institution of positive pressure ventilation, this further favors nondependent lung ventilation. Pulmonary perfusion is unaffected by muscle relaxation. However, the increase of P_A due to the institution of positive pressure ventilation will increase zone 1 ($P_A > P_{pa}$) and zone 2 territory ($P_A > P_{pv}$). The combination of reduced ventilation of the dependent lung and reduced perfusion of the nondependent lung disrupts V/Q matching beyond what was seen for the anesthetized, spontaneously breathing patient [2].

Open Chest

Opening of the chest, as well as the resulting loss of negative intrapleural pressure, releases the mediastinal weight onto the dependent lung, further worsening its compliance. The nondependent lung on the other hand is now free to move independent of chest-wall constraints, solely based on parenchymal compliance. Consequently, the lung will collapse, if lung

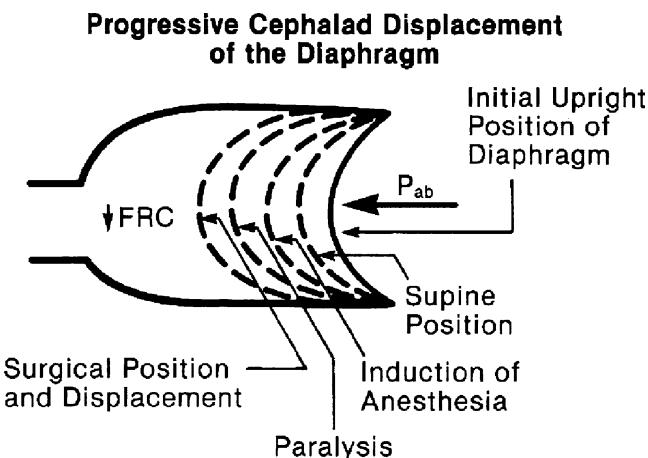


FIG. 5.11. Anesthesia and surgery result in progressive cephalad displacement of the diaphragm. All of, assuming the supine position, induction of anesthesia, paralysis, surgical positioning and retraction act to displace the diaphragm and decrease FRC (modified from Benumof [2]. © Elsevier 1995).

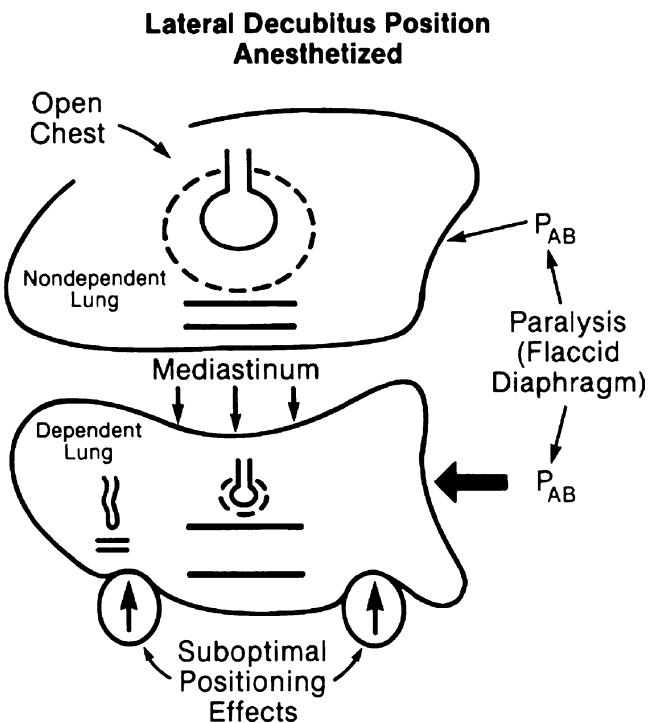


FIG. 5.12. Schematic summary of ventilation-perfusion relationships in the anesthetized patient in the lateral decubitus position. P_{AB} transmitted abdominal pressure (modified from Benumof [2]. © Elsevier 1995).

isolation has been applied, or will be able to herniate through the thoracotomy incision if still ventilated. The distribution of pulmonary blood flow will not be affected by opening the chest unless there is distortion of the mediastinal structures (Fig. 5.12). V/Q matching will depend on whether lung isolation is being employed. During TLV, opening of the chest will result in a deterioration of V/Q matching, due to increase in zone 1 ventilation when the nondependent lung is allowed

to herniate through the thoracotomy incision. Application of lung isolation, however, will divert all ventilation to the dependent lung, which already receives most of the perfusion, and therefore dramatically improves V/Q matching.

Most thoracic procedures are accomplished in the anesthetized, paralyzed and mechanically ventilated patient. As we have seen in the preceding sections, induction of anesthesia, lateral decubitus positioning, paralysis and mechanical ventilation result in progressive disruption of the close V/Q matching that is part of normal physiology. Pulmonary perfusion has remained rather undisturbed, with preferential perfusion of dependent areas. Conversely, ventilation has become progressively diverted to the nondependent lung, as the dependent lung experiences extrinsic compression by mediastinum and abdominal contents. The application of lung isolation forces ventilation back into the dependent lung and re-establishes relative V/Q matching in the dependent lung, at the expense of true shunt in the nondependent lung [2, 15].

Positions Other Than Lateral

Supine

Although not routine for thoracic surgery, a certain number of OLV cases are being performed in the supine position (e.g., chest-wall resections, sympathectomy, minimally invasive cardiac procedures). Lung compliance changes occur with induction of anesthesia, paralysis and mechanical ventilation, as previously described, however, unlike the lateral decubitus position, now affect each lung equally. Abdominal, and to some degree mediastinal, compression affects each lung. Pulmonary perfusion gradients are maintained in the supine position with preferential perfusion of dependent areas. As gravity affects both lungs equally the percentage of CO perfusing each lung is unaffected. V/Q matching is disturbed, with dependent areas receiving more perfusion, but less ventilation. Because of the minimal vertical distance from anterior to posterior compared to the lateral position, this disruption is relatively minimal in the supine position. However, initiation of OLV in the supine position is less well tolerated than in the lateral position. Because of the lack of gravity redistribution of blood flow, the shunt through the nonventilated lung is substantially larger than in the lateral decubitus position, resulting in worse oxygenation [31].

Prone

OLV in the prone position is rare; however, isolated reports of lung resection and minimally invasive esophagectomy in the prone position have been published [82–84]. The effects of prone positioning during TLV have been extensively investigated [85]. In contrast to the supine position, V/Q matching and FRC are better maintained, with secondary marked improvement in P_{aO_2} values. Lung compliance is improved, in part due to the lack of compression of lung tissue by mediastinal

structures [86]. The prone position lacks gravity redistribution of pulmonary blood flow similar to the supine position. The shunt fraction and oxygenation during OLV should therefore be comparable or better than the supine position, but worse than for the lateral position.

Summary

OLV is a well-established anesthetic technique, and it is increasingly being used to improve surgical exposure for a myriad of pulmonary and nonpulmonary intrathoracic procedures. Although well tolerated in the majority of patients, lung compliance and oxygenation are significantly impaired and may complicate the care of some patients. A thorough knowledge of pulmonary physiology explains the majority of the intra-operative trespasses that one encounters during OLV and enables appropriate interventions.

References

1. Maloney Jr JV, Schmutzner KJ, Raschke E. Paradoxical respiration and "pendelluft". *J Thorac Cardiovasc Surg*. 1961;41:291–8.
2. Benumof JL. Anesthesia for thoracic surgery. 2nd ed. Philadelphia: WB Saunders; 1994.
3. Tacconi F, Pompeo E, Fabbri E, Mineo TC. Awake video-assisted pleural decortication for empyema thoracis. *Eur J Cardiothorac Surg*. 2010;37(3):594–601.
4. Brodsky JB. The evolution of thoracic anesthesia. *Thorac Surg Clin*. 2005;15(1):1–10.
5. West JB. Respiratory physiology: the essentials. 5th ed. Baltimore: Williams and Wilkins; 1995.
6. Hakim TS, Lisbona R, Dean GW. Gravity-independent inequality in pulmonary blood flow in humans. *J Appl Physiol*. 1987;63(3):1114–21.
7. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. *J Appl Physiol*. 1964;19(4):713–24.
8. West JB, Dollery CT, Heard BE. Increased pulmonary vascular resistance in the dependent zone of the isolated dog lung caused by perivascular edema. *Circ Res*. 1965;17(3):191–206.
9. Chang H, Lai-Fook SJ, Domino KB, et al. Spatial distribution of ventilation and perfusion in anesthetized dogs in lateral postures. *J Appl Physiol*. 2002;92(2):745–62.
10. Groves BM, Reeves JT, Sutton JR, et al. Operation Everest II: elevated high-altitude pulmonary resistance unresponsive to oxygen. *J Appl Physiol*. 1987;63(2):521–30.
11. Maseri A, Caldini P, Harward P, Joshi RC, Permutt S, Zierler KL. Determinants of pulmonary vascular volume: recruitment versus distensibility. *Circ Res*. 1972;31(2):218–28.
12. Weir EK, Lopez-Barneo J, Buckler KJ, Archer SL. Acute oxygen-sensing mechanisms. *N Engl J Med*. 2005;353(19):2042–55.
13. Balanos GM, Talbot NP, Dorrington KL, Robbins PA. Human pulmonary vascular response to 4 h of hypercapnia and hypocapnia measured using Doppler echocardiography. *J Appl Physiol*. 2003;94(4):1543–51.
14. Nagendran J, Stewart K, Hoskinson M, Archer SL. An anesthesiologist's guide to hypoxic pulmonary vasoconstriction: implications for managing single-lung anesthesia and atelectasis. *Curr Opin Anaesthesiol*. 2006;19(1):34–43.
15. Grichnik KP, Clark JA. Pathophysiology and management of one-lung ventilation. *Thorac Surg Clin*. 2005;15(1):85–103.
16. Talbot NP, Balanos GM, Dorrington KL, Robbins PA. Two temporal components within the human pulmonary vascular response to approximately 2 h of isocapnic hypoxia. *J Appl Physiol*. 2005;98(3):1125–39.
17. Conacher ID. 2000 – time to apply occam's razor to failure of hypoxic pulmonary vasoconstriction during one-lung ventilation. *Br J Anaesth*. 2000;84(4):434–6.
18. Peinado VI, Santos S, Ramirez J, Roca J, Rodriguez-Roisin R, Barberà JA. Response to hypoxia of pulmonary arteries in chronic obstructive pulmonary disease: an in vitro study. *Eur Respir J*. 2002;20(2):332–8.
19. Nakos G, Evrenoglou D, Vassilakis N, Lampropoulos S. Haemodynamics and gas exchange in liver cirrhosis: the effect of orally administered almitrine bismesylate. *Respir Med*. 1993;87(2):93–8.
20. Reeves JT, Grover RF. Blockade of acute hypoxic pulmonary hypertension by endotoxin. *J Appl Physiol*. 1974;36(3):328–32.
21. Moore LG, Reeves JT. Pregnancy blunts pulmonary vascular reactivity in dogs. *Am J Physiol*. 1980;239(3):H297–301.
22. Wetzel RC, Zaczur HA, Sylvester JT. Effect of puberty and estradiol on hypoxic vasomotor response in isolated sheep lungs. *J Appl Physiol*. 1984;56(5):1199–203.
23. Favret F, Henderson KK, Allen J, Richalet JP, Gonzalez NC. Exercise training improves lung gas exchange and attenuates acute hypoxic pulmonary hypertension but does not prevent pulmonary hypertension of prolonged hypoxia. *J Appl Physiol*. 2006;100(1):20–5.
24. Guazzi MD, Berti M, Doria E, et al. Enhancement of the pulmonary vasoconstriction reaction to alveolar hypoxia in systemic high blood pressure. *Clin Sci (Lond)*. 1989;76(6):589–94.
25. Doekel RC, Weir EK, Looga R, Grover RF, Reeves JT. Potentiation of hypoxic pulmonary vasoconstriction by ethyl alcohol in dogs. *J Appl Physiol*. 1978;44(1):76–80.
26. Brimioule S, Lejeune P, Vachiery JL, Leeman M, Melot C, Naeije R. Effects of acidosis and alkalosis on hypoxic pulmonary vasoconstriction in dogs. *Am J Physiol*. 1990;258(2 Pt 2):H347–53.
27. Benumof JL, Wahrenbrock EA. Dependency of hypoxic pulmonary vasoconstriction on temperature. *J Appl Physiol*. 1977;42(1):56–8.
28. Benumof JL, Wahrenbrock EA. Blunted hypoxic pulmonary vasoconstriction by increased lung vascular pressures. *J Appl Physiol*. 1975;38(5):846–50.
29. Marshall C, Marshall B. Site and sensitivity for stimulation of hypoxic pulmonary vasoconstriction. *J Appl Physiol*. 1983;55(3):711–6.
30. Choi YS, Bang SO, Shim JK, Chung KY, Kwak YL, Hong YW. Effects of head-down tilt on intrapulmonary shunt fraction and oxygenation during one-lung ventilation in the lateral decubitus position. *J Thorac Cardiovasc Surg*. 2007;134(3):613–8.
31. Bardoczky GI, Szegedi LL, d'Hollander AA, Moures JM, De Francq P, Yernault JC. Two-lung and one-lung ventilation in patients with chronic obstructive pulmonary disease: the effects of position and FIO_2 . *Anesth Analg*. 2000;90(1):35–41.
32. Ishikawa S, Nakazawa K, Makita K. Progressive changes in arterial oxygenation during one-lung anaesthesia are related to the response to compression of the nondependent lung. *Br J Anaesth*. 2003;90(1):21–6.

33. Szegedi LL, Van der Linden P, Ducart A, et al. The effects of acute isovolemic hemodilution on oxygenation during one-lung ventilation. *Anesth Analg.* 2005;100(1):15–20.
34. Von Dossow V, Welte M, Zaune U, et al. Thoracic epidural anesthesia combined with general anesthesia: the preferred anesthetic technique for thoracic surgery. *Anesth Analg.* 2001;92(4):848–54.
35. Casati A, Mascotto G, Iemi K, Nzepa-Batonga J, De Luca M. Epidural block does not worsen oxygenation during one-lung ventilation for lung resections under isoflurane/nitrous oxide anaesthesia. *Eur J Anaesthesiol.* 2005;22(5):363–8.
36. Özcan PE, Sentürk M, Sungur Ulke Z, et al. Effects of thoracic epidural anaesthesia on pulmonary venous admixture and oxygenation during one-lung ventilation. *Acta Anaesthesiol Scand.* 2007;51(8):1117–22.
37. Moutafis M, Liu N, Dalibon N, et al. The effects of inhaled nitric oxide and its combination with intravenous almitrine on Pao_2 during one-lung ventilation in patients undergoing thoracoscopic procedures. *Anesth Analg.* 1997;85(5):1130–5.
38. Bindslev L, Cannon D, Sykes MK. Effect of lignocaine and nitrous oxide on hypoxic pulmonary vasoconstriction in the dog constant-flow perfused left lower lobe preparation. *Br J Anaesth.* 1986;58(3):315–20.
39. Kjaevel J, Bjertnaes LJ. Interaction of verapamil and halogenated inhalation anesthetics on hypoxic pulmonary vasoconstriction. *Acta Anaesthesiol Scand.* 1989;33(3):193–8.
40. Carlsson AJ, Hedenstierna G, Bindslev L. Hypoxia-induced vasoconstriction in human lung exposed to enflurane anaesthesia. *Acta Anaesthesiol Scand.* 1987;31(1):57–62.
41. Carlsson AJ, Bindslev L, Hedenstierna G. Hypoxia-induced pulmonary vasoconstriction in the human lung. The effect of isoflurane anaesthesia. *Anesthesiology.* 1987;66(3):312–6.
42. Kerbaul F, Guidon C, Stephanazzi J, et al. Sub-MAC concentrations of desflurane do not inhibit hypoxic pulmonary vasoconstriction in anesthetized piglets. *Can J Anaesth.* 2001;48(8):760–7.
43. Pruszkowski O, Dalibon N, Moutafis M, et al. Effects of propofol vs sevoflurane on arterial oxygenation during one-lung ventilation. *Br J Anaesth.* 2007;98(4):539–44.
44. Nakayama M, Murray PA. Ketamine preserves and propofol potentiates hypoxic pulmonary vasoconstriction compared with the conscious state in chronically instrumented dogs. *Anesthesiology.* 1999;91(3):760–71.
45. Bjertnaes L, Hauge A, Kriz M. Hypoxia-induced pulmonary vasoconstriction: effects of fentanyl following different routes of administration. *Acta Anaesthesiol Scand.* 1980;24(1):53–7.
46. Clozel JP, Delorme N, Battistella P, Breda JL, Polu JM. Hemodynamic effects of intravenous diltiazem in hypoxic pulmonary hypertension. *Chest.* 1987;91(2):171–5.
47. Thilenius OG, Candiolo BM, Beug JL. Effect of adrenergic blockade on hypoxia-induced pulmonary vasoconstriction in awake dogs. *Am J Physiol.* 1967;213(4):990–8.
48. Hackett PH, Roach RC, Hartig GS, Greene ER, Levine BD. The effect of vasodilators on pulmonary hemodynamics in high altitude pulmonary edema: a comparison. *Int J Sports Med.* 1992;13 Suppl 1:S68–71.
49. Lübbe N. The effect of clonidine on the intrapulmonary right-to-left shunt in one-lung ventilation in the dog. *Anesthesiol.* 1991;40(7):391–6.
50. Hales CA, Westphal D. Hypoxemia following the administration of sublingual nitroglycerin. *Am J Med.* 1978;65(6):911–8.
51. Parsons GH, Leventhal JP, Hansen MM, Goldstein JD. Effect of sodium nitroprusside on hypoxic pulmonary vasoconstriction in the dog. *J Appl Physiol.* 1981;51(2):288–92.
52. Zhao L, Mason NA, Morrell NW, et al. Sildenafil inhibits hypoxia-induced pulmonary hypertension. *Circulation.* 2001;104(4):424–8.
53. Marin JL, Orchard C, Chakrabarti MK, Sykes MK. Depression of hypoxic pulmonary vasoconstriction in the dog by dopamine and isoprenaline. *Br J Anaesth.* 1979;51(4):303–12.
54. Silove ED, Grover RF. Effects of alpha adrenergic blockade and tissue catecholamine depletion on pulmonary vascular response to hypoxia. *J Clin Invest.* 1968;47(2):274–85.
55. Doering EB, William Hanson III C, Reily DJ, Marshall C, Marshall BE. Improvement in oxygenation by phenylephrine and nitric oxide in patients with adult respiratory distress syndrome. *Anesthesiology.* 1997;87(1):18–25.
56. Hüter L, Schwarzkopf K, Preussler NP, et al. Effects of arginine vasopressin on oxygenation and haemodynamics during one-lung ventilation in an animal model. *Anaesth Intensive Care.* 2008;36(2):162–6.
57. Kiely DG, Cargill RI, Lipworth BJ. Acute hypoxic pulmonary vasoconstriction in man is attenuated by type I angiotensin II receptor blockade. *Cardiovasc Res.* 1995;30(6):875–80.
58. Cargill RI, Lipworth BJ. Lisinopril attenuates acute hypoxic pulmonary vasoconstriction in humans. *Chest.* 1996;109(2):424–9.
59. Leeman M, Lejeune P, Melot C, Deloof T, Naeije R. Pulmonary artery pressure: flow relationships in hyperoxic and in hypoxic dogs. Effects of methylprednisolone. *Acta Anaesthesiol Scand.* 1988;32(2):147–51.
60. Lorente JA, Landin L, de Pablo R, Renes E. The effects of prostacyclin on oxygen transport in adult respiratory distress syndrome. *Med Clin (Barc).* 1992;98(17):641–5.
61. Weir EK, Reeves JT, Grover RF. Prostaglandin E1 inhibits the pulmonary vascular pressor response to hypoxia and prostaglandin F2alpha. *Prostaglandins.* 1975;10(4):623–31.
62. Pillet O, Manier G, Castaing Y. Anticholinergic versus beta 2-agonist on gas exchange in COPD: a comparative study in 15 patients. *Monaldi Arch Chest Dis.* 1998;53(1):3–8.
63. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin.* 2008;26(2):241–72.
64. Gurney AM, Osipenko ON, MacMillan D, McFarlane KM, Tate RJ, Kempill FEJ. Two-pore domain K channel, TASK-1, in pulmonary artery smooth muscle cells. *Circ Res.* 2003;93(10):957–64.
65. Garutti I, Quintana B, Olmedilla L, Cruz A, Cruz A, Barranco M, Garcia de Lucas E. Arterial oxygenation during one-lung ventilation: combined versus general anesthesia. *Anesth Analg.* 1999;88(3):494–9.
66. Szegedi LL. Pathophysiology of one-lung ventilation. *Anesthesiol Clin North America.* 2001;19(3):435–53.
67. Levin AI et al. Arterial oxygenation during one-lung anaesthesia. *Curr Opin Anaesthesiol.* 2008;21:28–36.
68. Slinger P, Scott WA. Arterial oxygenation during one-lung ventilation. A comparison of enflurane and isoflurane. *Anesthesiology.* 1995;82(4):940–6.
69. Nomoto Y, Kawamura M. Pulmonary gas exchange effects by nitroglycerin, dopamine and dobutamine during one-lung ventilation in man. *Can J Anaesth.* 1989;36(3 Pt 1):273–7.
70. Mathru M, Dries DJ, Kanuri D, Blakeman B, Rao T. Effect of cardiac output on gas exchange in one-lung atelectasis. *Chest.* 1990;97(5):1121–4.

71. Russell WJ, James MF. The effects on arterial haemoglobin oxygen saturation and on shunt of increasing cardiac output with dopamine or dobutamine during one-lung ventilation. *Anaesth Intensive Care*. 2004;32(5):644–8.
72. Russell WJ, James MF. The effects on increasing cardiac output with adrenaline or isoprenaline on arterial haemoglobin oxygen saturation and shunt during one-lung ventilation. *Anaesth Intensive Care*. 2000;28(6):636–41.
73. Malmkvist G, Fletcher R, Nordström L, Werner O. Effects of lung surgery and one-lung ventilation on pulmonary arterial pressure, venous admixture and immediate postoperative lung function. *Br J Anaesth*. 1989;63(6):696–701.
74. McFarlane PA, Mortimer AJ, Ryder WA, et al. Effects of dopamine and dobutamine on the distribution of pulmonary blood flow during lobar ventilation hypoxia and lobar collapse in dogs. *Eur J Clin Invest*. 1985;15(2):53–9.
75. Benumof JL. Respiratory physiology and respiratory function during anesthesia. In: Miller RD, editor. *Anesthesia*. 2nd ed. New York: Churchill Livingstone; 1983.
76. Hoppin Jr FG, Green ID, Mead J. Distribution of pleural surface pressure in dogs. *J Appl Physiol*. 1969;27(6):863–73.
77. Milic-Emili J, Henderson JA, Dolovich MB, Trop D, Kaneko K. Regional distribution of inspired gas in the lung. *J Appl Physiol*. 1966;21(3):749–59.
78. West JB. Regional differences in gas exchange in the lung of erect man. *J Appl Physiol*. 1962;17(6):893–8.
79. Wulff KE, Aulin I. The regional lung function in the lateral decubitus position during anesthesia and operation. *Acta Anaesthesiol Scand*. 1972;16(4):195–205.
80. Rehder K, Hatch DJ, Sessler AD, Fowler WS. The function of each lung of anesthetized and paralyzed man during mechanical ventilation. *Anesthesiology*. 1972;37(1):16–26.
81. Rehder K, Wenthe FM, Sessler AD. Function of each lung during mechanical ventilation with ZEEP and with PEEP in man anesthetized with thiopental-meperidine. *Anesthesiology*. 1973;39(6):597–606.
82. Conlan AA, Moyes DG, Schutz J, Scocciati M, Abramor E, Levy H. Pulmonary resection in the prone position for suppurative lung disease in children. *J Thorac Cardiovasc Surg*. 1986;92(5):890–3.
83. Fabian T, Martin J, Katigbak M, McKelvey AA, Federico JA. Thoracoscopic esophageal mobilization during minimally invasive esophagectomy: a head-to-head comparison of prone versus decubitus positions. *Surg Endosc*. 2008;22(11):2485–91.
84. Turner MW, Buchanan CC, Brown SW. Paediatric one lung ventilation in the prone position. *Paediatr Anaesth*. 1997;7(5):427–9.
85. Albert RK. Prone ventilation. *Clin Chest Med*. 2000;21(3):427–9.
86. Pelosi P, Croci M, Calappi E, et al. The prone position during general anesthesia minimally affects respiratory mechanics while improving functional residual capacity and increasing oxygen tension. *Anesth Analg*. 1995;80(5):955–60.

6

Clinical Management of One-Lung Ventilation

Jens Lohser and Seiji Ishikawa

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Key Points

- Ventilation needs to be individualized for the underlying lung pathology.
- Ventilation is a modifiable risk factor for acute lung injury.
- Protective lung ventilation is a combination of small tidal volumes, low peak and plateau pressures, routine PEEP and permissive hypercapnea.
- Hypoxia during one-lung ventilation is rare and often secondary to alveolar de-recruitment in the face of hypoventilation.
- Management of hypoxia requires a structured treatment algorithm.

Introduction

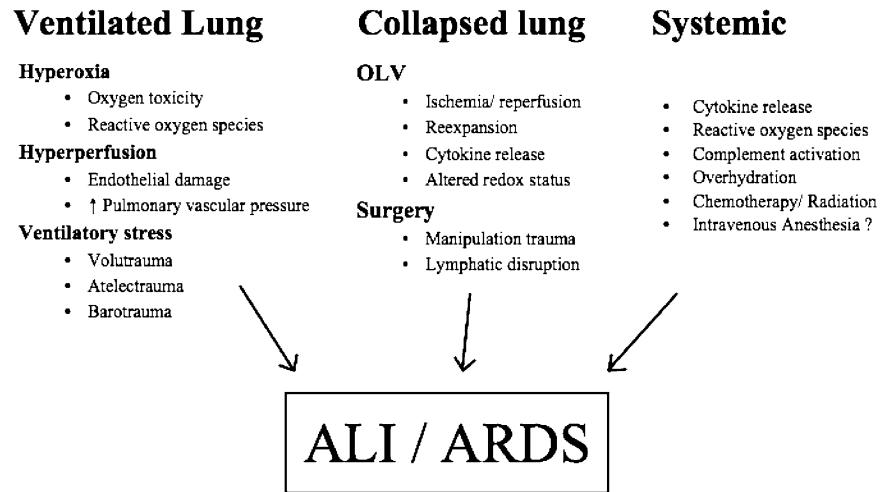
The development of thoracic surgery as a subspecialty only occurred after lung isolation and one-lung ventilation (OLV) had been reported. Prior to the description of endotracheal intubation and the cuffed endotracheal tube, only short intrathoracic procedures had been feasible. Rapid lung movement and quickly developing respiratory distress due to the surgical pneumothorax, made all but minimal procedures impossible. Selective ventilation of one lung was first described in 1931 by Gale and Waters and quickly led to increasingly complex lung resection surgery, with the first published pneumonectomy for cancer in 1933 [1]. Much has since been learnt about the physiology of OLV, particularly the issue of ventilation/perfusion matching (see Chap. 5). Hypoxemia used to be the primary concern during OLV. However, hypoxemia has become less frequent due to more effective lung isolation techniques,

particularly the routine use of fiberoptic bronchoscopy (FOB), and the use of anesthetic agents with little or no detrimental effects on hypoxic pulmonary vasoconstriction (HPV). Acute lung injury (ALI) has replaced hypoxia as the chief concern associated with OLV [2].

Acute Lung Injury

Lung injury after lung resection was first recognized in the form of postpneumonectomy pulmonary edema [3], which is now referred to as post-thoracotomy ALI [4]. Pneumonectomy carries a particularly high risk of lung injury, but lesser lung resections and even nonpulmonary intra-thoracic surgery which employs OLV can create the same pathology [5]. Post-thoracotomy ALI is part of a spectrum of disease, which in its most severe form is recognized as acute respiratory distress syndrome (ARDS). Diagnosis is based on the oxygenation index of $P_{a}O_2/F_{i}O_2$ (P/F). Critical care consensus guidelines define ALI as a P/F ratio <300 and ARDS as a P/F ratio <200 [6]. ALI after lung resection is fortunately infrequent, occurring in 2.5–3.1% of all lung resections combined; however, the incidence can be as high as 7.9–10.1% after pneumonectomies. Although infrequent, ALI after lung resection may be associated with significant morbidity in the form of prolonged intubation, hospitalization and death [5]. Mortality, which was reported to be as high as 37–64% amongst patients with ALI [7–9], may be on the decline, as a more recent report indicated a mortality rate of 25–40% [10]. Similarly, Tang et al. reported a decrease in both incidence of (3.2 to 1.6%) and mortality from (72 to 45%) ARDS after pulmonary resection in a single institution cohort over a 10-year period. Their data

FIG. 6.1. Proposed mechanisms for ALI and ARDS after lung resection surgery.



have to be interpreted with caution, however, as the number of pneumonectomies was drastically higher in the historical cohort (17.4 versus 6.4%), which may explain the higher morbidity and mortality [11].

The etiology of lung injury is likely multifactorial (Fig. 6.1). Early on risk factors were felt to be right-sided surgery and large perioperative fluid loads. However, impaired lymphatic drainage, surgical technique, ventilation, transfusion, aspiration, infection, oxidative stress and ischemia–reperfusion have all since been implicated [12]. The fact that ventilation may have detrimental effects in the critically ill patients in the form of ventilator-induced lung injury has long been recognized. Early animal studies demonstrated that high tidal volumes (45 mL/kg) are particularly injurious to the lung, irrespective of the applied pressure. This has led to the term “volutrauma” and the realization that end-inspiratory stretch plays a dominant role in lung injury [13]. In ARDS patients, application of protective lung ventilation (PLV) with smaller tidal volumes and high positive end-expiratory pressure (PEEP) improved survival [14]. Additionally, protective ventilation was shown to inhibit progression of lung injury compared to high tidal volume ventilation [13]. Whether mechanical ventilation causes lung injury in normal lungs and whether protective ventilation should routinely be applied in anesthesia is being debated. Tidal volume reduction towards 6 mL/kg for patients with risk factors for lung injury, and no higher than 10 mL/kg for the remainder, have been proposed for routine two-lung ventilation (TLV) [15, 16]. Considering that most patients undergoing thoracic surgery have risk factors for lung injury (Table 6.1), tidal volume reduction during TLV, and even more so during OLV should become routine practice.

The application of OLV predisposes the patient to ALI. Radiologic density changes in patients with ALI after thoracic surgery are more pronounced in the nonoperative, ventilated lung [17]. An increased duration of OLV was found to be an independent predictor of ALI in a retrospective analysis [7]. In animal models, OLV causes histological changes compatible with lung injury, including vascular congestion, diffuse

TABLE 6.1. Risk factors for ALI after OLV.

Patient	Poor postoperative predicted lung function Preexisting lung injury Trauma Infection Chemotherapy EtOH abuse Female gender
Procedure	Prolonged OLV (>100 min) Lung transplantation Larger resections (pneumonectomy > lobectomy) Esophagectomy Transfusion Large perioperative fluid load

alveolar wall thickening and damage, as well as a decrease in nitric oxide in the ventilated lung [18, 19]. Re-expansion of lung tissue after short-term OLV incites pro-inflammatory cytokine release in animals [20]. Similar cytokine elevations are found in patients undergoing thoracic surgery [21, 22]. Much of the early attention focused on the use of high tidal volumes during OLV. The analogy to ARDS has been drawn, as both involve ventilation of a so-called “baby lung” with reduced lung capacities [23]. Analogous to ARDS, high tidal volumes may therefore cause excessive end-inspiratory stretch during OLV.

Beyond ventilatory management, even anesthetic agents themselves appear to have the potential to modify the inflammatory response to OLV and surgery. De Conno et al. allocated adult patients undergoing lung resection surgery into propofol or sevoflurane anesthesia, and found that the increase in inflammatory mediators during OLV was significantly less pronounced in the sevoflurane group. Composite adverse events were significantly higher in the propofol group, but the groups differed in OLV duration and the need for surgical re-exploration [24]. The possible benefit of inhalational

anesthesia is not without merit, as volatile anesthetics have been shown to confer attenuating effects in a model of alveolar epithelial injury [25]. In another study, which compared desflurane or propofol anesthesia in thoracic surgery patients, levels of alveolar TNF α and sICAM-1 were significantly higher in the propofol group [26]. These studies indicate that anesthetic agents themselves may influence the pro-inflammatory response to OLV, but the true clinical relevance of that decrease remains to be established. Not surprisingly, however, the true answer as to lung injury avoidance after OLV is likely more complicated than simple tidal volume reduction.

Ventilator Settings

Tidal Volume

Tidal volumes used during TLV (10–12 mL/kg) used to be maintained into the period of OLV [27, 28]. Large tidal volumes were recommended because they had been found to improve oxygenation and decrease shunt fraction, during both TLV [29] and OLV, irrespective of the level of PEEP applied [30]. Large tidal volumes were shown to provide end-inspiratory alveolar recruitment, resulting in improved oxygenation (Fig. 6.2). Excessive tidal volumes (e.g., 15 mL/kg), on the other hand, were shown to worsen oxygenation, secondary to elevations in pulmonary vascular resistance (PVR) resulting in increased shunt flow [31]. Based on the recent literature on ALI, it is becoming increasingly clear that large tidal volumes during OLV expose the patient to undue risk of postoperative respiratory complications.

Two retrospective case series by Van de Werff and Licker identified multiple risk factors among more than 1,000 patients undergoing lung resection surgery. Both studies demonstrated a significant association between high ventilating pressures and ALI, but failed to provide a link to intraoperative tidal volumes [7, 32]. Fernández-Pérez et al., on the other hand, showed a significant association between larger intraoperative tidal volumes (8.3 vs. 6.7 mL/kg) and the development of postoperative respiratory failure in a single institution review of 170 pneumonectomies [33]. The study was criticized for the fact that ventilatory pressures were not analyzed, tidal volumes referred to the largest volume charted on the anesthetic record, with the assumption that they had been carried over to OLV, and patients that developed respiratory failure received a median of 2.2 L of fluid intraoperatively [34]. However, the results were essentially duplicated in another single-institution review of 146 pneumonectomy patients. In that study, larger tidal volumes were independently associated with the development of ALI/ARDS (8.2 vs. 7.7 mL/kg) with an odds ratio (OR) of 3.37 per one mL/kg increase in tidal volume per predicted body weight (95% confidence interval 1.65–6.86). Peak airway pressure was an additional independent risk factor with an OR 2.32 per cm H₂O increase (95% confidence interval 1.46–3.67) [35].

One of the earliest trials of tidal volume reduction during OLV was an animal study published in 2003 [36]. Isolated rabbit lungs were subjected to OLV with either 8 mL/kg – zero end-expiratory pressure (ZEEP) or the “protective” 4 mL/kg – average PEEP 2.1 cmH₂O (based on the dynamic pressure-time curve). OLV was associated with increases in multiple surrogate markers of lung injury (pulmonary artery pressure [PAP], lung weight gain [LWG] and TXB₂ cytokine levels), which occurred to a lesser degree in the protective ventilation group. The protective ventilation group, however, only received half the minute ventilation of the control group, as no compensatory increase in respiratory rate was used in the low tidal volume group. Based on the study design it was therefore not possible to state whether the outcome benefit was due to any one, or all, of minute ventilation reduction, tidal volume reduction and/or application of external PEEP [36]. Kuzkov et al. showed that when comparing equal minute ventilation in anesthetized sheep undergoing pneumonectomies, protective ventilation with 6 mL/kg – PEEP 2 cmH₂O lowered extravascular lung water (a surrogate for lung injury), compared to 12 mL/kg – ZEEP [37]. While neither study was able to answer the question whether tidal volume reduction or the addition of PEEP results in improved outcomes, it appears clear that tidal volume reduction alone is not sufficient. This point was well illustrated by an animal study comparing low vs. high tidal volume ventilation with or without PEEP in ALI. While animals with high tidal volume ventilation and ZEEP clearly had significant cytokine elevations, all animals exposed to low tidal volumes and ZEEP died during the experiment [38].

Due to the infrequent occurrence of lung injury, prospective clinical studies have focused on cytokine levels as a surrogate marker for potentially harmful ventilation. Cytokine elevations are part of the disease process, as levels of IL-6, IL-8, sICAM-1 and vWF are elevated even prior to intubation in patients with ALI [39] and baseline plasma levels of IL-6, IL-8 and IL-10 are associated with an increased risk of death in patients with ARDS [40]. Wrigge et al. failed to demonstrate a difference in tracheal cytokine levels between patients ventilated with 12–15 mL/kg – ZEEP or 6 mL/kg – PEEP 10 cmH₂O during TLV and OLV for laparotomy or thoracotomy. Cytokine levels before, during and after OLV were no different between the groups [41]. However, tracheal aspirates may not be sensitive enough to detect early alveolar damage. Michelet randomized 52 patients with normal lung functions undergoing esophagectomy to OLV 9 mL/kg – ZEEP or 5 mL/kg – PEEP 5 cmH₂O. In this study, serum cytokine levels (IL-1, IL-6, IL-8) increased perioperatively, but to a lesser degree in the protective ventilation group [22]. The degree of lung injury and cytokine elevation may have been exaggerated by the fact that despite an average of 6 h of mechanical ventilation and 8 L of fluid, only the low tidal volume group received PEEP during OLV and no patient received PEEP during the remainder of the operation [22]. Esophageal surgery may also present a higher risk for lung injury as it is associated with cytokine elevations secondary to intestinal ischemia, potentially acting as a first hit [42].

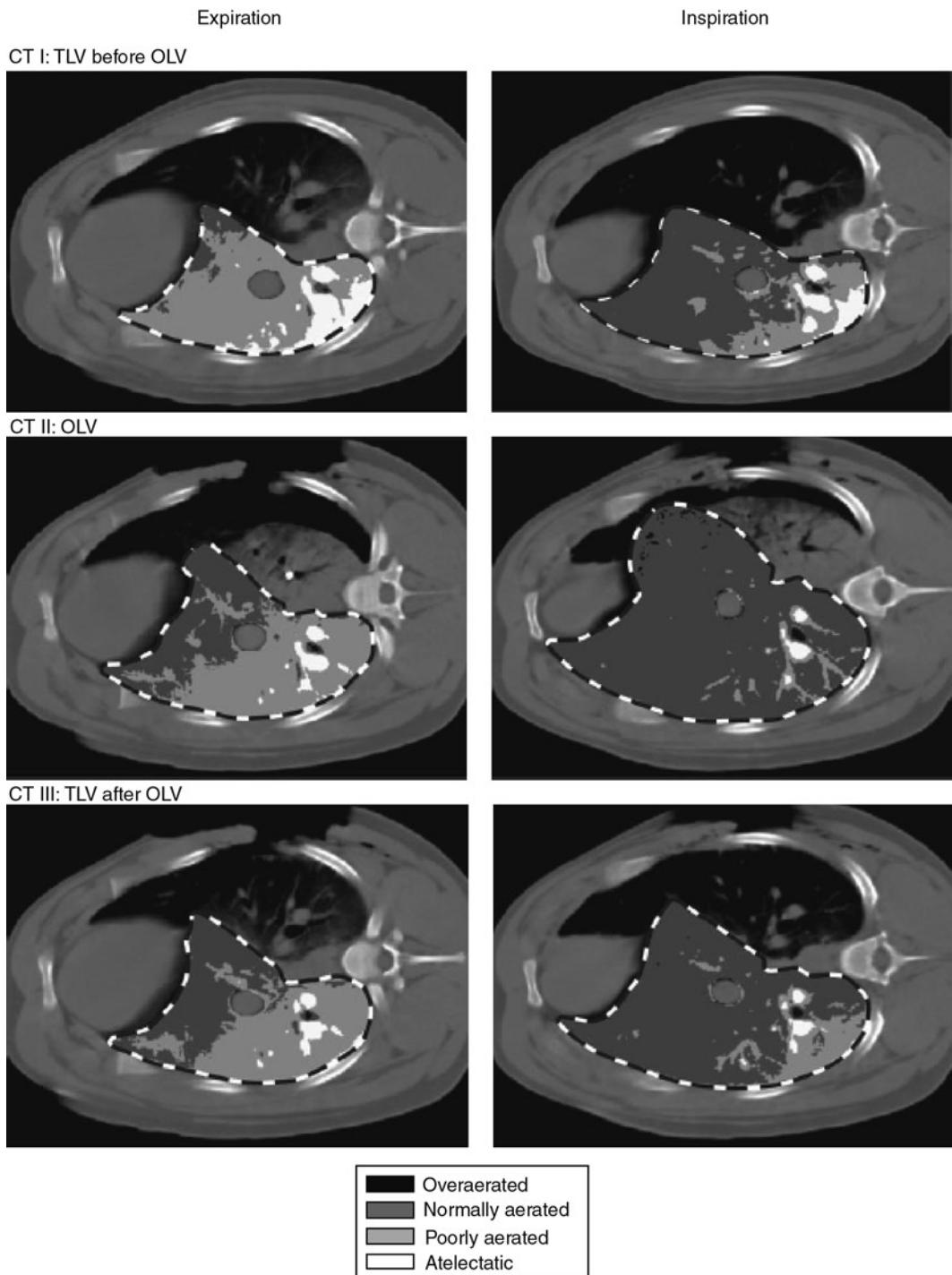


FIG. 6.2. Juxta-diaphragmatic lung CT images of a porcine one-lung ventilation (OLV) model. Scans during two-lung ventilation (TLV) before OLV (CT I), during OLV (CT II), and TLV after OLV (CT III). Lung aeration was defined based on image scaling units (Hounsfield); over-aerated (-1,000 to -900 HU), normally aerated (-900 to -500 HU), poorly aerated (-500 to -100 HU), and atelectatic (-100 to +100 HU) lung regions are coded by gray scale. The dependent lung border is outlined by the *dashed line* (reprinted from Kozian et al. [120], with permission).

The most compelling experimental evidence that tidal volumes per se are linked to the etiology of ALI after lung surgery comes from a randomized trial, which investigated 32 patients scheduled for OLV and thoracotomy. Patients received OLV

with 10 or 5 mL/kg, both without PEEP but identical minute ventilation. While OLV increased cytokine levels (TNF- α , sICAM-1) in both groups, levels were lower in the low tidal volume ventilation group [21].

More important than cytokine elevations, clinically significant outcomes of ALI, ICU admission and hospital stay were shown to be reduced in a cohort analysis of patients who routinely received PLV (2003–2008), as compared to historical controls (1998–2003) [44]. While historical controls are fraught with limitations due to concomitant developments and improvements in medical care, this analysis by Licker et al. showed a dramatic reduction in adverse postoperative respiratory outcomes after the routine implementation of a PLV strategy. The ventilation strategy consisted of an open lung concept, with tidal volumes <8 mL/kg, routine PEEP, pressure-control ventilation (PCV) and frequent recruitment maneuvers. The statistically averaged ventilation parameters among the 558 patients in their protective ventilation group consisted of a tidal volume of 5.3 mL/kg (standard deviation [SD] 1.1), plateau pressure of 15 cmH₂O (SD 6), PEEP of 6.2 cmH₂O (SD 2.4) and respiratory rate of 15 bpm (SD 2). While the historical control already had a mean tidal volume of 7.1 mL/kg, only 24% of patients received tidal volumes less than 8 mL/kg, compared to the 92% compliance with low tidal volumes in the PLV cohort. As mentioned above, historical comparisons of ICU admission and length of hospitalization are difficult to interpret as criteria change and moves towards fast-tracking of patients are established. However, the definition of ALI has been consistent during the study period and the authors were able to show a significant reduction in ALI from 3.8 to 0.9% [44].

While the benefits of protective ventilation for lung injury prevention are becoming clearer, its impact on oxygenation is uncertain. Two studies that investigated PLV (lower tidal volume and PEEP) during OLV reported improved oxygenation and shunt fraction as compared to traditional high tidal volume OLV [22, 37]. However, with inadequate or no PEEP, low tidal volume ventilation may be associated with worse oxygenation and shunt fraction [21]. Recruitment studies performed during protective OLV have shown that despite a PEEP of 8 cmH₂O patient ventilated with a tidal volume of 6 mL/kg showed significant recruitability of the ventilated lung, suggesting relative hypoventilation and atelectasis formation. Despite the presence of atelectatic lung prior to the recruitment maneuver, however, oxygenation was adequate in all patients [43]. Postoperative arterial oxygenation was not affected in a historical cohort analysis of patients undergoing lung cancer surgery with a PLV protocol incorporating lower tidal volumes [44].

PEEP

Positive-end expiratory pressure minimizes alveolar collapse and atelectasis formation by providing resistance to mechanical exhalation. Applied PEEP should therefore be routine for all ventilated patients during TLV [15]. Klingstedt et al. demonstrated that the mediastinal weight results in significant compression of the dependent lung in the lateral position during TLV. They were able to show that resulting *V/Q* mismatch

can be resolved with the application of selective PEEP to the dependent lung (Fig. 6.3) [45].

PEEP does attenuate lung injury, both in the setting of high and low tidal volumes [13]. Intrinsic or auto-PEEP, on the other hand, occurs if expiratory time is too short to allow lung units to empty towards their resting volume. Lung areas with high compliance, characteristically found in patients with emphysema, are particularly prone due to their poor elastic recoil. Auto-PEEP is inhomogeneous throughout the lung and can therefore not be relied upon for effective avoidance of de-recruitment [46]. The total PEEP after application of external PEEP is also unpredictable, due to the heterogeneous nature of auto-PEEP [47].

Endotracheal intubation prevents glottic closure, resulting in complete absence of auto-PEEP in patients without obstructive lung disease on TLV. However, initiation of OLV with 10 mL/kg ZEEP has been shown to create auto-PEEP and air trapping. Measured auto-PEEP was minimal in patients without obstructive lung disease, but patients with severe COPD developed auto-PEEP levels up to 16 cmH₂O, which was associated with air trapping of 284 mL [46]. Patients with preexisting auto-PEEP have an unpredictable response to the application of extrinsic PEEP. In a study of ICU patients on TLV, application of PEEP changed total PEEP up, down or not at all [48]. In a small study of patients during OLV the additive effect of applied PEEP to auto-PEEP was inversely related to the preexisting auto-PEEP level. In other words, extrinsic PEEP contributed less to total PEEP in patients with already high auto-PEEP than patients with low auto-PEEP; however, the extent of the response was not predictable [47]. Excessive total PEEP and dynamic hyperinflation are clearly undesirable as they may cause cardiovascular depression and may require fluid loading and/or inotropic support [16].

Traditionally OLV has been performed with ZEEP, with selective application of PEEP to the nonoperative lung as part of a hypoxemia treatment algorithm. The effect of PEEP on oxygenation during OLV is variable. It is beneficial in patients whose intrinsic PEEP is well below the lower inflection point (LIP) of the compliance curve, more commonly the patient with normal lung function. In that scenario application of external PEEP will increase the total PEEP towards the LIP of the pressure–volume curve, resulting in more open (recruited) lung and improved oxygenation. Oxygenation is worse, however, if total PEEP is increased well above the LIP, likely due to alveolar over-distention and increases in PVR resulting in an increased shunt fraction (Fig. 6.4) [49]. Neither intrinsic PEEP nor the compliance curve is routinely or easily acquired during thoracic surgery, which is why preoperative prediction of PEEP responders would be ideal. Valenza et al. showed that patients with relatively normal lung function (FEV₁>72%) exhibited improved oxygenation on application of PEEP 10 cmH₂O during OLV [50].

Whether applied PEEP is able to decrease ALI after OLV is unclear, as it has not been studied in isolation. PEEP application as part of a “protective” ventilation regime has

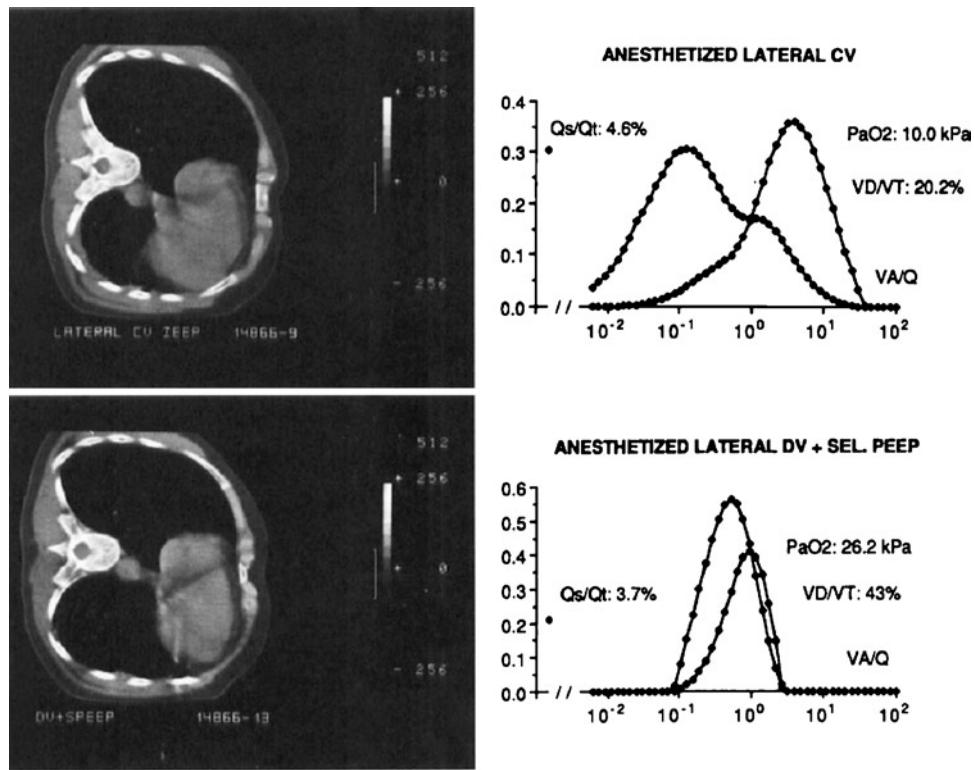


FIG. 6.3. Mediastinal weight causes significant dependent lung compression and secondary ventilation/perfusion (V/Q) mismatch during two-lung conventional ventilation (CV). Application of differential ventilation (DV) and selective PEEP (SPEEP) to the dependent lung restores V/Q matching. For comparison see Fig. 4.7a for a normal awake V/Q scan (reprinted from Klingstedt et al. [45], with permission).

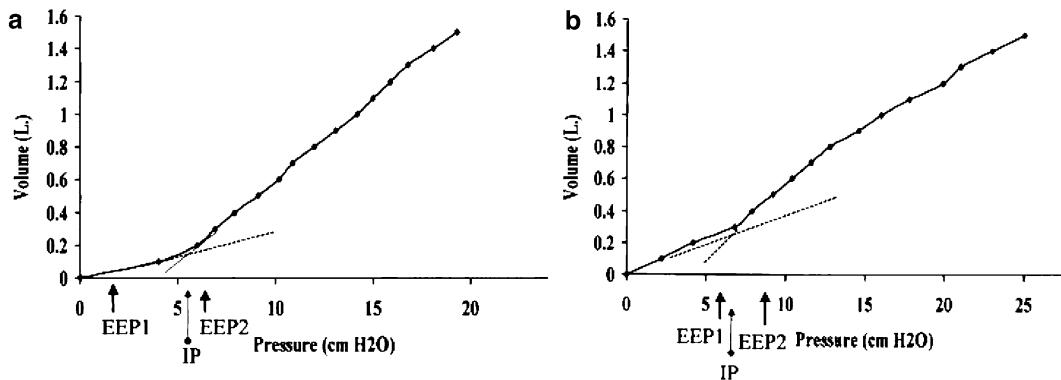


FIG. 6.4. Effect of applied PEEP on total PEEP and oxygenation during OLV. Static compliance curves of patients undergoing OLV. End-expiratory pressure before (EEP1) and after application of 5 cmH_2O PEEP (EEP2) as well as lower inflection points (IP) are indicated. Patients with normal pulmonary function and low EEP1 (a), in whom EEP2 moved closer to IP were more likely to show oxygenation benefits after PEEP application, than patients with poor lung function and intrinsic PEEP (b). See text for details (reprinted from Slinger et al. [49], with permission).

been shown to decrease surrogate markers of lung injury [22, 36, 37]. Additionally, routine PEEP in patients with or without COPD as part of a PLV strategy was shown to be associated with a significant decrease in the incidence of ALI and atelectasis after OLV [44].

Use of “protective” OLV with low tidal volumes but no PEEP does not appear sensible, as de-recruitment is harmful and auto-PEEP unreliable in terms of homogeneous lung recruitment. Lack of PEEP in the setting of low tidal volume OLV has been shown to worsen oxygenation [21].

Low levels of PEEP are safe, likely beneficial for lung injury avoidance and should be used in all patients. The only true contraindication to PEEP application would be the presence of a broncho-pleural fistula. PEEP levels, however, need to be adjusted to the individual and their respiratory mechanics. Patients with normal lung function or restrictive lung disease should benefit from, and will tolerate, 5–10 cmH₂O PEEP. Patients with severe obstructive lung disease, as evidenced by preoperative hyperinflation (RV/TLC>>140%) exhibit significant air trapping during OLV, but as previously stated may not exhibit a significant increase in total PEEP with the application of external PEEP. Low levels of extrinsic PEEP 2–5 cmH₂O are likely well tolerated and should routinely be applied. Clearly dynamic hyperinflation must be considered in the differential for intraoperative hypotensive episodes in patients at risk. However, based on the static compliance analysis by Licker et al., who used routine PEEP in all patients as part of their PLV strategy, hyperinflation (and secondary decrease in static compliance) does not appear to be a significant concern, as the compliance actually increased in their cohort exposed to PLV with routine PEEP [44]. Early, routine application of PEEP helps to prevent atelectasis and shunt formation and thereby improves oxygenation during OLV [51].

Clearly it would be best to measure total PEEP for each patient in order to rationally apply external PEEP [47]. This, however, is difficult or impossible in most intraoperative settings due to the inability of anesthetic ventilators to perform an end-expiratory hold maneuver. The simplest approximation of intrinsic PEEP can be derived from inline spirometry where interruptions of the end-expiratory flow curve indicate the presence of auto-PEEP (Fig. 6.5) [52]. Alternatively, compliance can be approximated by simple calculation (compliance=tidal volume/driving pressure), which may serve as an indicator of potential air-trapping, realizing that hyperinflation is only one of the possible explanations for a decrease in compliance.

F_iO₂

One hundred percent oxygen used to be a routine component of OLV, as hypoxia was its most feared complication. However, with the decline in the incidence of hypoxemia and the realization that high F_iO₂ may be detrimental, even this practice has been questioned. Oxygen toxicity is a well-recognized consequence of prolonged exposure to high F_iO₂, characterized by histopathologic changes similar to ALI. Oxygen toxicity occurs during OLV and involves ischemia–reperfusion injury and oxidative stress [12]. Collapse of the operative lung and surgical manipulation results in relative organ ischemia, and reperfusion at the time of lung expansion leads to the production of radical oxygen species. Increasing durations of OLV and the presence of tumor result in increased markers of oxidative stress, which after 120 min are associated with significant increases in the rates of respiratory failure and death [53]. Lung re-expansion should likely occur at a lower F_iO₂, as hypoxic reperfusion has been shown to attenuate the reperfusion syndrome [54]. This is of particular relevance after lung transplantation. Even short-term exposure to high F_iO₂ during the induction of anesthesia has been shown to cause significant absorption atelectasis [55]. Studies have shown that an F_iO₂ as low as 0.4 may provide adequate oxygenation for OLV in the lateral decubitus position [56]. Due to the potential for lung injury, particularly in the high-risk patient, after adjuvant therapy or undergoing lung transplantation, F_iO₂ should be titrated to effect. At the initiation of OLV a F_iO₂ of 0.8 may be appropriate, but 15–20 min later, when the nadir of oxygenation has occurred, the F_iO₂ should be gradually decreased to the minimum that is required to maintain a stable saturation level above 92–94%. During lung resection surgery further reductions in F_iO₂ are possible once the vasculature to the resected lobe or lung has been disrupted. Stapling of the vasculature effectively reduces, or, in the setting of a pneumonectomy, essentially eliminates the shunt flow.

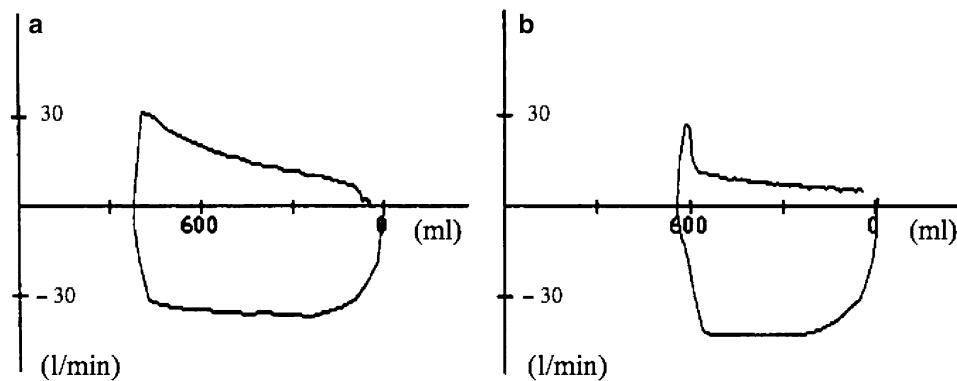


FIG. 6.5. Auto-PEEP detection by in-line spirometry. Flow volume curves with expiration above and inspiration below the line. Expiratory flow normally returns to zero prior to inspiration (a), interrupted air-flow at end-expiration indicates the presence of auto-PEEP (b) (reprinted from Dueck et al. [121] with permission).

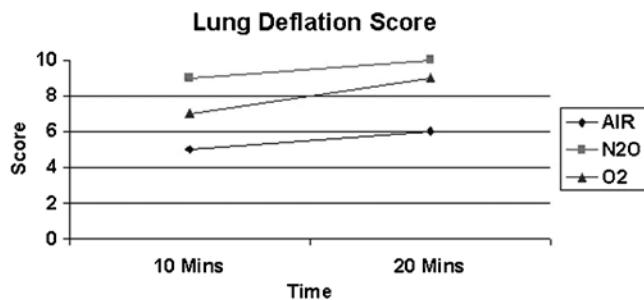


FIG. 6.6. Lung deflation is significantly impaired when nitrogen is part of the gas mixture pre-OLV (reprinted from Ko et al. [57], with permission).

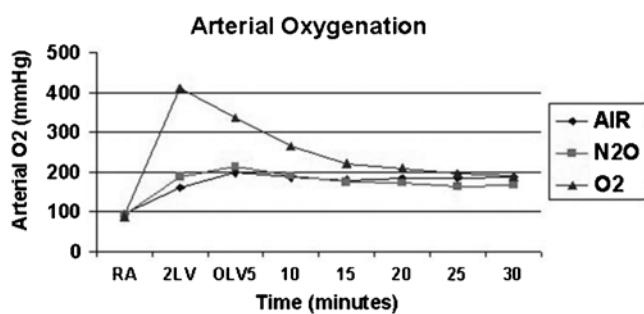


FIG. 6.7. Use of 100% O₂ pre-OLV confers a transient oxygenation benefit, which is lost by 15 min of OLV (reprinted from Ko et al. [57] with permission).

The oxygen content and gas mixture are not only important for oxygenation, but also for the speed of nonventilated lung collapse during OLV. This is of particular importance for surgical exposure during video-assisted thoracoscopic surgery. Ko et al. compared three different gas mixtures during TLV immediately prior to OLV (air/O₂, N₂O/O₂, O₂) and investigated which gas mixture would best collapse the operative lung while maintaining arterial oxygenation in patients undergoing lung resection surgery [57]. F_{O2} was 0.4 in the air/O₂ and N₂O/O₂ group, and 1.0 in the O₂ group during TLV. All groups received 100% oxygen on initiation of OLV. Not surprisingly, lung deflation was worse if nitrogen (i.e., air) was administered prior to lung collapse, due to the poor solubility of nitrogen in blood (Fig. 6.6). A nitrous oxide/O₂ mixture was superior to oxygen alone for lung collapse, but nitrous oxide is contraindicated in many thoracic patients. Administering 100% oxygen pre-OLV temporarily improved OLV oxygenation, but only until the nonventilated lung becomes atelectatic. Once the operative lung has collapsed at around 15 min of OLV that oxygen reservoir and any benefit from it has disappeared (Fig. 6.7) [57].

Minute Ventilation/Permissive Hypercapnea

Permissive hypercapnia has been a key component of the critical care management for ALI/ARDS. Reduction of

the minute ventilation allows for a decrease in tidal volumes and ventilatory pressures, thereby minimizing mechanical stress and secondary volu- or barotrauma. Beyond the reduction in minute ventilation and mechanical trauma, the actual elevated CO₂ level itself may be beneficial [58], as hypercapnia appears to attenuate the cytokine response [59].

Permissive hypercapnia has been investigated in the OLV setting. In the previously mentioned study by Gama de Abreu et al., isolated rabbit lungs were exposed to OLV with 8 mL/kg – ZEEP or 4 mL/kg – PEEP 2.1 cmH₂O (based on the dynamic pressure-time curve), without respiratory rate compensation. The protective ventilation group, which received half the minute ventilation, exhibited a reduction in surrogate markers for lung injury (PAP, LWG, cytokine levels) [36]. Similar ventilatory parameters were studied during OLV in thoracotomy patients. Sticher et al. ventilated patients with 7 mL/kg – PEEP 2 cmH₂O or 3.5 mL/kg – PEEP 2 cmH₂O, again without respiratory rate compensation, effectively halving minute ventilation similar to Gama de Abreu. P_aCO₂ values rose from 42 to 64 mmHg, which was associated with a 42% increase in PVR, but no change in oxygenation. Hypercapnia was well tolerated, however, higher risk patients with pulmonary hypertension or major cardiac rhythm disturbances were excluded [60]. In a case series of 24 patients undergoing volume reduction surgery for advanced emphysema, permissive hypercapnia was used electively as part of a barotrauma avoidance strategy. The mean P_aCO₂ value was 56 mmHg with a peak of 86 mmHg, resulting in pH values between 7.11 and 7.41 (mean 7.29). The authors state that hypercapnia was well tolerated, however, inotropic support was required in over 50% of patients [61]. Even higher P_aCO₂ levels have been described in a small series of ten patients with severe emphysema that were again managed with elective hypoventilation for barotrauma avoidance. P_aCO₂ values rose to peak levels of 70–135 mmHg, resulting in pH values as low as 7.03 (despite bicarbonate administration). Hypercapnia was poorly tolerated at these high levels. All patients required inotropic support during anesthesia. Four patients developed ventricular dysrhythmias and three patients required tracheal gas insufflation for treatment of hypoxemia [62]. Significant hypercapnia can cause increased intracranial pressure, pulmonary hypertension, decreased myocardial contractility, decreased renal blood flow and release of endogenous catecholamines. At extremely high levels, CO₂ can be lethal due to excessive sympathetic stimulation, cardiac rhythm disturbances and/or cardiac collapse [16, 62]. Moderate hypercapnia potentiates the HPV response and is therefore unlikely to adversely affect oxygenation [63]; however, the same may not hold true for extreme CO₂ elevations [62]. A protective ventilation strategy including permissive hypercapnia has been shown to reduce the incidence of ALI in a cohort analysis by Licker et al. While not explicitly discussed in the manuscript, permissive hypercapnia clearly was part of their strategy. The PLV group had significantly lower tidal volumes with only marginal rate compensation. Based on the

manuscript, the minute ventilation of the historical cohort was 92 vs. 80 mL/kg/min in the PLV group. The PLV group therefore had smaller minute ventilation and increased anatomic dead space ventilation (increased respiratory rate), resulting in decreased CO_2 elimination [44]. Permissive hypercapnea should be considered a routine component of a PLV strategy for OLV. Assuming a reasonable cardiovascular reserve, and in particular right ventricular function, P_aCO_2 levels up to 70 mmHg are well tolerated in the short term and clearly beneficial in terms of lung injury avoidance and attenuation. Higher levels should be avoided in the majority of patients due to the risk of hemodynamic instability.

I:E Ratio and Respiratory Rate

Each ventilatory cycle consists of time spent in inspiration and expiration. The appropriate ratio of inspiratory to expiratory (I:E) time depends on underlying lung mechanics. Restrictive lung disease is characterized by poorly compliant lungs, which resist passive lung expansion, but rapidly recoil to FRC. Increasing the I:E ratio to 1:1 (or using inverse ratio ventilation) maximizes the time spent in inspiration, thereby reducing peak and plateau ventilatory pressures. For illustration, at a respiratory rate of 15 bpm and an I:E ratio of 1:1, each respiratory cycle lasts 4 s, with 2 s spent in each of inspiration and expiration, respectively. Obstructive lung disease, on the other hand, is characterized by lungs, which have difficulty to empty towards FRC, due to poor elastic recoil and conducting airway collapse. Decreasing the I:E ratio towards 1:4 allows for more expiratory time, and helps to minimize the risk of auto-PEEP and dynamic hyperinflation. For illustration, at a respiratory rate of 15 bpm, now with the I:E ratio to 1:4, each respiratory cycle is still 4 s, however, expiration now takes up 3.2 s of the entire cycle.

Respiratory rate modification may be equally necessary depending on the underlying lung mechanics. Extreme airflow obstruction may require very long expiratory times. After reducing the I:E ratio to the minimum of 1:4 this can only be achieved by increasing the overall cycle length, i.e., reducing the respiratory rate. Clinical examples, such as the patient with severe cystic fibrosis requiring a respiratory rate of 4–6 to allow for complete exhalation have been reported [64]. In restrictive lung disease, on the other hand, dividing a given minute volume by a higher respiratory frequency may be beneficial in reducing peak and plateau ventilatory pressures. It has to be realized, however, that as anatomic dead space remains unchanged, dividing the minute volume by a higher respiratory rate results in reduced CO_2 elimination as the unchanged size of the anatomic dead space makes up a larger component of the tidal volume [65]. For illustration, a patient ventilated at 400 mL – 20 bpm receives the identical minute ventilation as a patient ventilated at 800 mL – 10 bpm. However, dead space ventilation, which occupies about 150 mL of each breath, has doubled from 1,500 mL at 10 bpm to 3,000 mL at 20 bpm. Alveolar ventilation has therefore been reduced from 6,500 mL

(8,000–1,500) to 5,000 mL (8,000–3,000). Additionally, OLV with small tidal volume and rapid respiratory rate results in statistically higher auto-PEEP [65]. While auto-PEEP elevations in this study were unlikely to be clinically significant, they serve as a reminder that rapid, shallow ventilation has the potential to increase dynamic hyperinflation.

Peak/Plateau Pressure

The peak inspiratory pressure is a reflection of the dynamic compliance of the respiratory system and depends on tidal volume, inspiratory time, endotracheal size and airway tone (bronchospasm). Plateau pressure, on the other hand, relates to the static compliance of the respiratory system, i.e., chest wall and lung compliance. Double-lumen endobronchial tubes have small internal diameters resulting in increased resistance to air flow [66]. Application of the full TLV minute volume to a single lumen of the double lumen tube (DLT) results in a 55% increase in peak inspiratory pressure and 42% increase in plateau pressure [67]. While plateau pressure reflects alveolar pressure, peak pressure is unlikely to be fully applied to the alveolus. A retrospective study of 197 pneumonectomy patients did, however, show that peak ventilation pressures above 40 cmH_2O were associated with the development of PPPE [32]. Recently, Fernández-Pérez et al. reviewed 4,420 consecutive patients without preexisting lung injury undergoing high-risk elective surgeries for postoperative pulmonary complications and demonstrated that mean first hour airway pressure (OR 1.07; 95% CI 1.02–1.15 cmH_2O) but not tidal volume, PEEP or F_iO_2 , were associated with ALI after adjusting for nonventilatory parameters [68]. Similarly, patients exposed to a plateau pressure of 29 cmH_2O were at significantly higher risk of developing ALI after lung resection surgery than those with a plateau pressure of 14 cmH_2O [7]. Based on the critical care literature there does not appear to be a critical plateau pressure level above which injury occurs, but rather any elevation in plateau pressure increases the relative risk of lung injury. With the implementation of permissive hypoventilation, peak pressure levels well less than 35–40 cmH_2O and plateau pressures less than 25 cmH_2O should therefore be achievable in the majority of patients during OLV. This was confirmed in the cohort study by Licker et al. who showed that implementation of a PLV strategy for OLV resulted in mean plateau pressures of 15 cmH_2O [44].

Ventilatory Mode

Volume-control ventilation (VCV) has been the dominant ventilatory mode both in the intensive care and operating room. VCV uses a constant inspired flow (square wave), creating a progressive increase in airway pressure towards the peak inspiratory pressure, which is reached as the full tidal volume has been delivered. Inspiratory pressure during VCV depends on the set tidal volume and PEEP, gas flow rates and resistance, as well as respiratory system compliance. The set

tidal volume will be delivered unless the inspiratory pressure exceeds the pressure limit, in which case the flow ceases. With the realization that ventilatory pressures may be one of the inciting factors of lung injury, other ventilatory modes have been explored.

PCV uses a decelerating flow pattern, with maximal flow at the beginning of inspiration until the set pressure is reached, after which flow rapidly decreases balancing the decreasing compliance of the expanding lung. This resembles the spontaneous mammalian breath which also follows a decelerating pattern, as negative intrathoracic pressure induced by contracting diaphragm and intercostal muscles cause a high initial air-flow [15]. Tidal volumes can be highly variable during PCV and may fall precipitously with changes in lung compliance, such as with surgical manipulation. As the majority of the tidal volume is delivered in the early part of the inspiration, mean airway and alveolar pressure tend to be higher during PCV. The decelerating flow pattern results in a more homogeneous distribution of the tidal volume, improving static and dynamic lung compliance due to recruitment of poorly ventilated lung regions, and improving oxygenation and dead-space ventilation [69]. Whether PCV during OLV improves oxygenation is controversial. Tu rul et al. studied 48 patients undergoing thoracotomy and lung resection. Patients received VCV or PCV during OLV, both delivering 10 mL/kg – ZEEP –100% O₂, in a cross-over fashion. PCV was associated with statistically significant decreases in peak and plateau airway pressures, as well as improved oxygenation and shunt fraction. Oxygenation improved more in patients with poor preoperative lung function, which may relate to the more homogeneous distribution of ventilation achieved with the pressure-control breath [70]. The same group investigated the benefit of adding PEEP 4 cmH₂O to OLV with PCV and showed that it provided an additional significant improvement in oxygenation and shunt fraction in their patients [71]. Other groups, however, have failed to reproduce the oxygenation benefit in PCV studies during OLV [72–74].

The effect of intraoperative ventilatory mode on postoperative oxygenation is equally controversial. Although a better postoperative oxygenation was shown in the PCV group compared with VCV in a trial of patients undergoing MIDCAB surgery [75], no significant difference was demonstrated in a study of patients after thoracic surgery [76]. Despite the lack of a clear oxygenation benefit, PCV is likely preferable over VCV due to the potential to decrease ventilatory pressures and the ability to recruit lung units.

High-frequency jet ventilation (HFJV) is another ventilatory mode that has been successfully used in thoracic surgery [77]. HFJV, when applied to the operative lung during prolonged OLV in aortic surgery, is more effective than continuous positive airway pressure (CPAP) in improving P_aO₂ [78]. This may be particularly relevant in the poor operative candidate after prior contra-lateral lung resection [79]. One recent study evaluated the value of two-lung HFJV via a standard endotracheal tube for thoracic surgery. Sixty patients were

randomized to HFJV (1 atm pressure, rate 200/min, 100% O₂) or standard OLV (10 mL/kg, 100% O₂, ZEEP). HFJV was associated with lower ventilating pressures, improved oxygenation and shunt fraction and importantly no detriment in surgical exposure or intraoperative hemodynamic variables [80]. More recently, Buise et al. reported that HFJV was associated with a lower mean blood loss and less crystalloids administration during esophagectomy, compared with the OLV group. They speculated that higher ventilatory pressures in the OLV group resulted in higher intrathoracic pressure and central venous pressure, and thus splanchnic congestion, which increased blood loss relative to the HFJV group [81]. Difficulties in monitoring ventilatory pressures, tidal volumes and end-tidal CO₂ concentrations, in addition to the inherent risks of barotrauma associated with this technique, continue to limit its widespread adoption [77].

Another ventilatory mode, which has only been used as a CPAP equivalent at this point, is high-frequency percussive ventilation (HFPV). It is a ventilatory technique providing convective and diffusive ventilation that can reduce the physiologic right-to-left shunt and improve arterial oxygenation [82–84]. Lucangelo et al. recently assessed the effects of HFPV (F_iO₂ 1.0, 500 cycles/min, mean pressure 5 cmH₂O, with pressures oscillating between 2 and 8 cmH₂O) applied to the nondependent lung compared to standard CPAP in patients undergoing elective lung resection. Before nondependent lung re-expansion, HFPV patients showed higher P_aO₂ than CPAP. HFPV was also associated with better clearance of secretions and shortened hospital stay [85].

Recruitment/Re-Expansion

Atelectasis has long been known to occur in dependent lung areas of anesthetized patients. The primary reasons for alveolar collapse during anesthesia are extrinsic compression and gas resorption. Recent studies have shown that atelectatic alveoli are not simply air-less, but may also be fluid or foam-filled. Beyond simple lung collapse, atelectasis is therefore now considered both a potential cause and a manifestation of ALI [55]. Interestingly, re-expansion of collapsed alveoli causes injury not only to the alveoli that are being recruited, but also to remote nonatelectatic alveoli [55]. This may be in part to the early realization by Mead that expansion of a gas-free alveolus with a trans-pulmonary pressure of 30 cmH₂O creates a shear force of 140 cmH₂O to adjacent alveoli [13]. PEEP has been shown to prevent lung injury associated with both high and low tidal volumes, by stabilizing alveoli, and preventing their collapse [55]. In animal models of ARDS it has been shown that atelectasis is associated with vascular leak, right ventricular failure and eventual death in 31% of rats, and is easily avoided with PEEP [86].

Atelectasis formation in the nonoperative lung is highly undesirable during OLV as it worsens the already high shunt fraction, increasing the potential for hypoxemia. Among the risk factors that predispose to lung de-recruitment during

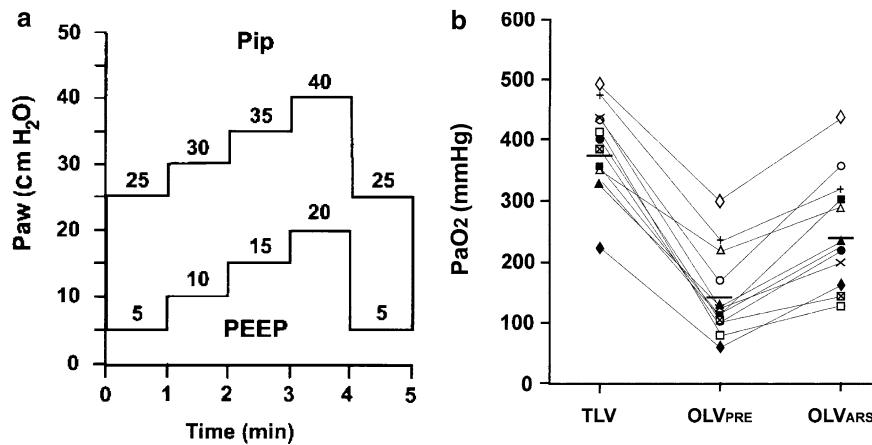


FIG. 6.8. Lung recruitment improves oxygenation during OLV. (a) Schematic representation of the ARM. In PCV, the pressure amplitude of 20 cmH₂O remains constant throughout the maneuver. Respiratory rate is 12 bpm and I:E ratio 1:1. Each pressure step is maintained for 1 min. After recruitment pressures of 40/20 cmH₂O, pressures decreased to 30/10 cmH₂O. Then, the initial settings are resumed (paw airway pressure; Pip peak inspiratory pressure). (b) P_aO₂ (mmHg) in all patients during two-lung ventilation (TLV) and during one-lung ventilation before (OLV_{PRE}) and after (OLV_{ARS}) the (ARM). Each symbol represents one patient in every point of the study. Horizontal bars represent mean values at each point (reprinted from Tusman et al. [43], with permission).

OLV are high F_iO₂, traditional lack of PEEP and extrinsic compression by abdominal contents, heart and mediastinum. The best evidence for the presence of atelectasis during OLV comes from a lung recruitment study, which investigated an aggressive alveolar recruitment maneuver (ARM) with increasing pressure breaths over a 4-min period up to a peak pressure of 40 cmH₂O and a PEEP level of 20 cmH₂O (Fig. 6.8a). Recruitment increased P_aO₂ on OLV from a mean of 144 mmHg to a mean of 244 mmHg (Fig. 6.8b) [43].

Cinnella et al. demonstrated that the alveolar recruitment achieved by such an ARM resulted in a significant decrease in static elastance of the dependent lung [87]. Hemodynamic instability is a well-recognized risk of such an aggressive ARM as the sustained intrathoracic pressure increases right ventricular afterload, resulting in impaired venous return and left heart preload [88, 89]. A recent study showed that stroke volume variation (an indicator of preload responsiveness) increases dramatically after an ARM, while both cardiac index and venous oxygen saturation decrease. These changes, however, were transient and completely recovered within 3 min [90].

Caution is required with the implementation of PLV, as low tidal volumes and plateau pressures may promote atelectasis formation and increase F_iO₂ and PEEP requirements [16]. Frequent de-recruitment and therefore need for repeated recruitment maneuvers, as may be the case with low tidal volume ventilation with insufficient PEEP, are potentially deleterious. In animal models of lung injury, repeated de-recruitment and recruitment maneuvers are associated with histological evidence of lung injury [91, 92]. Even a single recruitment maneuver of 40 cmH₂O for 40 s has been shown to elevate biomarkers of lung injury in the rat model without preexisting lung injury [93]. The same may potentially be true in humans, although this aspect has only been studied in critically ill patients.

Halbertsma et al. demonstrated that a single ARM could increase translocation of pro-inflammatory cytokines from the alveolar space into the systemic circulation in ventilated critically ill children. Fifteen minutes after the ARM, an increase was observed in plasma TNF α , IL-6 and IL-1 β [94]. Another critical care study found that 4 out of 28 patients with ALI/ARDS developed barotrauma necessitating intervention following an ARM [95]. This does create a curious dilemma as the increased use of PLV, with low tidal volumes, may promote atelectasis formation and therefore increase the need for recruitment maneuvers [16]. The best ventilatory strategy is therefore one that follows the “open lung” concept and maintains lung recruitment.

Atelectasis formation in the operative lung is routine and occurs gradually over a 10–20 min period as residual oxygen is being absorbed, which parallels the gradual decline in P_aO₂ on OLV. Ko et al. compared three different gas mixtures during TLV immediately prior to OLV (air/O₂, N₂O/O₂, O₂) and investigated which gas mixture would best collapse the operative lung while maintaining arterial oxygenation in patients undergoing lung resection surgery. F_iO₂ was 0.4 in the air/O₂ and N₂O/O₂ group, and 1.0 in the O₂ group during TLV. All groups received 100% oxygen on initiation of OLV. Not surprisingly, lung deflation was worse if nitrogen (i.e., air) was administered prior to lung collapse, due to the poor solubility of nitrogen in blood (Fig. 6.6). A nitrous oxide/O₂ mixture was superior to oxygen alone for lung collapse, but nitrous oxide is contraindicated in many thoracic patients. Administering 100% oxygen pre-OLV temporarily improved OLV oxygenation, but only until the nonventilated lung becomes atelectatic. Once the operative lung has collapsed at around 15 min of OLV, that oxygen reservoir and any benefit from it has disappeared (Fig. 6.7) [57].

Atelectasis is complete, unless CPAP is applied to the operative lung. CPAP, or its variant HFJV, if applied to the at least partially recruited operative lung, effectively improves *V/Q* matching and hypoxemia [78]. Gradual re-expansion of the operative lung at the conclusion of OLV is achieved with a continuous pressure hold of 20–30 cmH₂O, which is lower than standard recruitment regimens, in order to prevent disruption of staple lines. As discussed, re-expansion of lung tissue may be harmful. Re-expansion injury after prolonged lung collapse consists of alveolar-capillary membrane edema and increase in lymphocyte and neutrophil infiltration [96]. Re-expansion of isolated rabbit lungs after 55 min of lung collapse showed significant elevations in myeloperoxidase (MPO) levels, as well as IL-1 β and TNF- α mRNA, when compared to an open lung control [20]. Intermittent lung re-expansion may mitigate these effects, as intermittent recruitment of the operative lung during OLV has been shown to decrease pro-inflammatory mediators during esophagectomy [97]. Lung recruitment with continuous high pressure hold may result in significant hypotension if applied to both lungs. However, even in the setting of hypovolemia, recruitment is well tolerated, if it is selectively applied to one lung at a time, with the other lung open to atmosphere [98]. Re-expansion pulmonary edema is fortunately rare if a gradual, gentle recruitment technique is applied, and is more likely after sudden recruitment of long-standing lung collapse [99]. Yet, even a single recruitment maneuver has the potential to cause lung injury in animal models [93]. Low oxygen tensions should likely be used for re-expansion, as recruitment of the operative lung is associated with substantial oxidative stress, particularly after prolonged OLV [53, 54].

OLV Duration

Mechanical stress due to OLV can be minimized by optimization of ventilatory parameters. However, even minimal stress using “protective” parameters becomes significant if exposure is prolonged. Retrospective case series have shown that OLV lasting more than 100 min is associated with an increased risk for postoperative lung injury [7]. Part of the damage may be due to oxidative stress. A recent animal study exposed rats to increasing durations of OLV from 1 to 3 h. At the conclusion of the experiment animals were sacrificed and analyzed for biochemical indicators of oxidative stress and histologic changes in lung tissue. Increasing the duration of OLV from 1 to 3 h resulted in significant elevations of malondialdehyde (MDA) activity and increased the amount of tissue damage on histological analysis [100]. A prospective analysis of patients undergoing lobectomy for nonsmall cell cancer with either TLV or OLV lasting more than 60, 90 or 120 min compared MDA plasma levels at lung re-expansion. Again, MDA levels increased significantly with increasing OLV duration, indicating cumulative oxidative stress [53]. Anesthesiologists have limited control over the duration of OLV as it is mostly determined by the surgical procedure. However, initiation of OLV should occur as close to pleural opening as possible (except

for thoracoscopic procedures), and TLV should resume as early as possible. With the increasing use of OLV outside the thoracic theater, it is essential to ensure that the nonthoracic surgeon appreciates the need to minimize the length of OLV.

Ventilatory Strategy

The cumulative evidence is overwhelmingly in favor of adopting a protective lung ventilatory strategy for OLV, which has been shown to decrease surrogate markers of lung injury as well as the incidence of ALI itself. Protective ventilation is not synonymous with low tidal volume ventilation, but includes all of routine PEEP, lower FiO₂ and particularly lower ventilatory pressures through the use of PCV and permissive hypercapnea. This strategy follows the “open-lung” concept that has been widely adopted for management of ARDS patients in intensive care units. As part of the open-lung concept frequent recruitment of the lung has to be considered as another component of a PLV strategy. Recruitment should occur at the beginning of OLV, during OLV if indicated by worsening oxygenation and for lung re-expansion. Lung de-recruitment may potentially be more prevalent with low tidal volumes due to the loss of end-inspiratory stretch in the setting of high F_iO₂. External PEEP should help to minimize de-recruitment. However, PEEP titration is difficult in the intra-operative setting for two reasons. First, determination of inflection points and auto-PEEP would require inline spirometry, as routine expiratory holds are not feasible intra-operatively. Second, other than the ICU, where as long as cardiac output is maintained, PEEP can be increased to maintain “open lung”; in the OLV setting excessive PEEP will cause pulmonary blood flow diversion to the operative lung and worsens oxygenation. As such, low tidal volume ventilation has the potential to worsen oxygenation, either due to lung de-recruitment with inadequate PEEP or due to pulmonary blood flow diversion with excessive PEEP. Low tidal volume ventilation increases dead-space and CO₂ elimination is therefore consistently worse with this technique. This should not present a problem in the majority of patients, unless CO₂ elimination is already compromised by severe obstructive lung disease (e.g., cystic fibrosis). In cases of severe respiratory acidosis, marked pulmonary hypertension or right ventricular dysfunction, “protective” low-tidal volume – high rate ventilation may need to be aborted in favor of higher tidal volume ventilation at a lower respiratory rate (to maximize CO₂ elimination), as the imminent risk of hemodynamic dysfunction trumps the potential risk of ALI. Dynamic hyperinflation is common during OLV and is increased with the application of PEEP and the use of higher respiratory rates. The risk of hyperinflation may be increased with a PLV strategy, which has to be considered, particularly in patients with severe emphysema and during periods of hemodynamic instability. Providing adequate expiratory time and use of permissive hypoventilation should minimize the risk of significant hyperinflation in all but the patients with severe obstructive lung.

TABLE 6.2. Summary of ventilatory strategies.

Tidal volume: protective: 4–6 mL/kg; hypoxia or severe hypercapnea: consider 6–8 mL/kg
PEEP: protective/restrictive/normal: 5–10 cmH ₂ O; obstructive: 2–5 cmH ₂ O (minimize intrinsic PEEP)
RR: protective: 12–15 bpm; severe hypercapnea: 6–8 bpm
F _i O ₂ : transplant: 21%+, routine 50–80%, hypoxia 100%
I:E ratio: restrictive: 1:1 or inverse ratio; normal: 1:2; obstructive: 1:3–4
Pressures: plateau <20 cmH ₂ O, peak <35 cmH ₂ O
Minute volume: P _a CO ₂ 50–70 mmHg (rarely higher: severe obstruction, lung transplantation)
Ventilator mode: PCV (? HFJV)

While PLV should be the norm for all patients, it is particularly important in patients with risk factors for ALI and during procedures that trigger a higher inflammatory response, such as pneumonectomy, esophageal surgery or lung transplantation. Respiratory mechanics vary widely between restrictive and obstructive lung disease so that any ventilatory strategy needs to be individualized for the particular patient (Table 6.2).

Hypoxia

Prediction

Hypoxia used to be the major concern during OLV. Early reports indicated that 40–50% of patients suffered hypoxemia during OLV [101]. Predictors for possible desaturation have been identified (Table 6.3). Hurford et al. examined the intraoperative oxygenation of patients who had undergone preoperative *V/Q* scanning [101]. They found that the amount of preoperative perfusion (and ventilation) to the operative lung inversely correlated with P_aO₂ after 10 min of OLV. As HPV is only able to halve blood flow through the operative lung during OLV, the authors concluded that the extent of preoperative blood flow helped to predict the amount of intra-operative shunt. Slinger et al. showed that P_aO₂ during OLV relates to multiple factors. Poor oxygenation during TLV was predictive of continued oxygenation difficulties as were right-sided operations (due to the increased perfusion to that side). Good preoperative pulmonary function (FEV₁) was found to be predictive of poor OLV oxygenation, which is felt to be due to the lack of auto-PEEP and secondary de-recruitment in normal lungs [102]. Two recent studies correlated the risk of hypoxemia to the end-tidal CO₂ gradients. One study showed that the difference of end-tidal CO₂ between the lungs in the lateral position significantly correlates with the P/F ratio at 15 min of OLV [103]. The other study demonstrated that there was a significant negative correlation between the lowest P_aO₂ recorded during the first 45 min of OLV and the end-tidal CO₂ difference between TLV and the early phase of OLV [104]. Both studies postulated that elevated CO₂ gradients were indicative of *V/Q* mismatching and therefore explained the risk of hypoxemia.

Over the years the incidence of hypoxemia has been declining. Improvements in anesthetic technique including

TABLE 6.3. Predictors of hypoxemia during one-lung ventilation.

Preferential perfusion of the operative lung
Right-sided surgery
Prior contralateral resection
Supine position
Normal FEV ₁
Poor oxygenation on TLV
High A-a gradient for CO ₂

TABLE 6.4. Approach to hypoxemia during one-lung ventilation.

Mild hypoxemia (90–95%)
Confirm position of lung isolation device
Recruit ventilated lung
Ensure adequate cardiac output
Increase F _i O ₂ towards 1.0
Optimize PEEP to nonoperative lung (up or down; towards lower inflection point)
CPAP/HFJV/O ₂ insufflation to operative lung (IPAP, FOB)
Consider reduction in vapor anesthetic and/or total intravenous anesthesia
Ensure adequate oxygen carrying capacity (hemoglobin)
Severe (<<90%) or refractory hypoxemia
Resume TLV with 100% O ₂
If not possible, consider
Pulmonary artery clamp on operative side during pneumonectomy, transplant
Inhaled NO and/or infusions of almitrine/phenylephrine
Extracorporeal support during lung transplantation (Nova-lung, CPB)

improved lung isolation, confirmation of lung isolation with FOB and use of anesthetic agents with less effects on HPV are being credited for the reduction of oxygenation difficulties. In 1993 the incidence of hypoxia <90% occurring during OLV was quoted at 9% [105]. By 2003 the published incidence of hypoxemia was down to 1% of OLV cases in some hands [106]. However, another more recent study again showed a 10% incidence of hypoxemia <90% in a single institution between 2003 and 2004. The discrepancy could be due to variations in clinical management. Alternatively, it may indicate the difference between manual and electronic charting, as the latter study consisted of automatic recording of saturation every 30 s [107]. Although rare, significant hypoxia may still occur, at times without warning [108].

Treatment

For a rational approach to hypoxia during OLV it has to be appreciated that CPAP and TLV are uniformly effective (Table 6.4). CPAP always decreases shunt flow and TLV essentially eliminates shunt flow. Aside from procedures such as pneumonectomy and lung transplantation where these techniques are not available, patients should therefore not have to suffer prolonged hypoxemia. Assuming that the lung isolation device is properly positioned, these two maneuvers are the most effective treatments for hypoxemia. They are not chosen as first-line interventions, however, because they will impair surgical access to the lung, particularly during thoracoscopic procedures.

CPAP is easily applied via one of the commercially available units that connect to the open lumen of the DLT, or the suction port of the bronchial blocker via the CPAP adaptor (Fig. 6.9). Alternatively, a standard AMBU bag with a PEEP valve can be used if no CPAP unit is available. CPAP does require some degree of lung recruitment, which is not always feasible (lung lavage, bronchopleural fistula) and will impact surgical exposure. Recently, Russell et al. described an intermittent positive airway pressure (IPAP) technique, which does not elicit lung inflation and therefore should not impact surgical exposure (Fig. 6.10). While the technique does not call for lung recruitment, it is unlikely to be of benefit in the setting of complete



FIG. 6.9. Commercially available CPAP unit connected to the open lumen of a double-lumen tube. Flow rate is constant at 5 L/m of oxygen via wall outlet. CPAP pressure can be dialed in between 1 and 10 cmH₂O.

lung collapse. It is based on intermittent delivery of short bursts of low-flow oxygen (2 L/min) to the nonventilated lung to treat hypoxemia, circumventing significant lung movement in the surgical field. Placing a standard bacteriostatic filter on the open lumen of the DLT, with oxygen connected to the CO₂ sampling port, manual occlusion of open filter end allows for “jet-insufflation” of oxygen into the collapsed lung. A 2-s burst of flow will deliver 66 mL of oxygen to the nonventilated lung. In this study, all of the ten patients with relative hypoxemia (SpO₂ < 95%) were successfully treated by repeated 2-s bursts of oxygen, followed by 10-s exhalations and no surgical interference was noted [109].

Hypoxemia during OLV for VATS presents a particular problem, as TLV and CPAP techniques are generally considered to be contraindicated. Ku et al. presented a novel method, which may be of benefit in select cases. They described the treatment of refractory hypoxemia during left-sided VATS for lung volume reduction surgery. A 4-mm FOB was inserted into the basilar segment of the left lower lobe bronchus and 5 L/min of oxygen was insufflated for approximately 20 s via the suction port (Fig. 6.11). Oxygenation successfully recovered within 2 min without impairing the surgical field and remained adequate for 20 min. There are two important considerations to this technique. First, it can only be applied if the insufflation occurs in a lung territory that is remote to the surgical site, and is therefore unlikely to be successful in case of a central lesion. In this case report, oxygen was insufflated into basilar segments while lung resection occurred at the apex. Second, insufflation of relatively high-flow oxygen has the potential to cause lung over-distention or barotrauma if the bronchoscope tip is allowed to wedge in the airway. The authors guarded against this by having the surgeon visualize the basilar lung

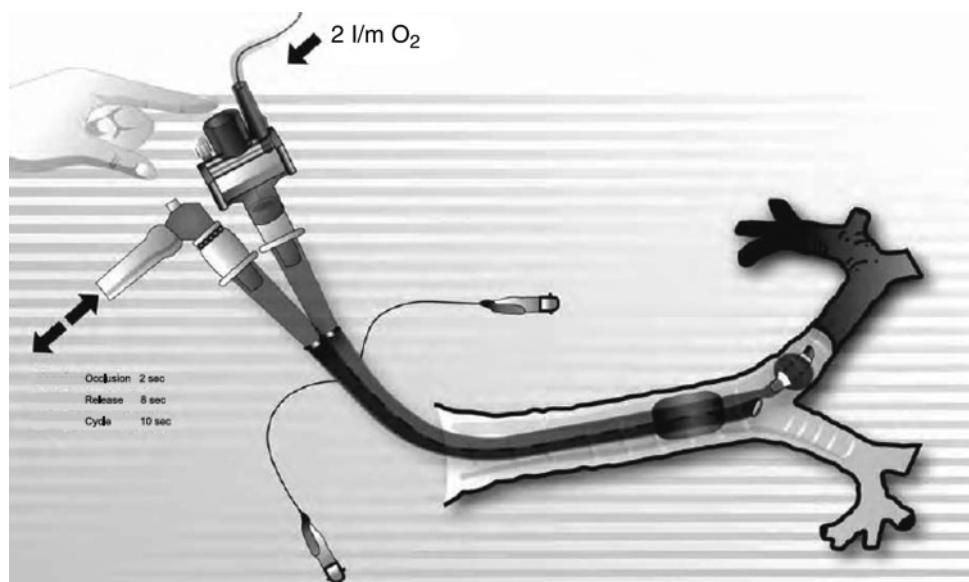


FIG. 6.10. Schematic illustration of intermittent positive airway pressure device. See text for details (reprinted from Russell [109], with permission).

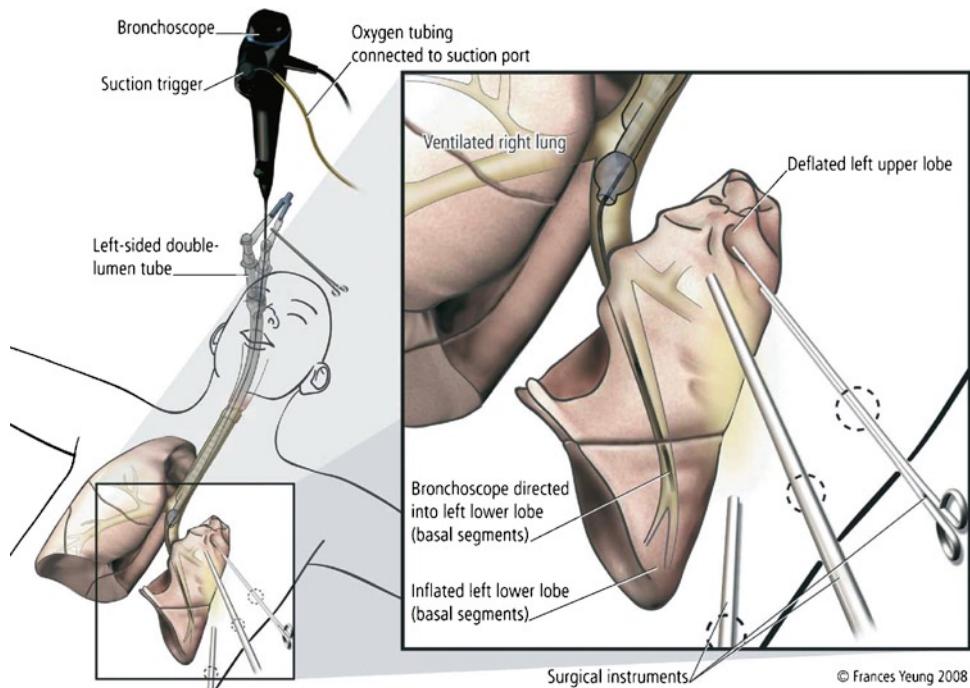


FIG. 6.11. Schematic illustration of oxygen supplementation during thoracoscopic surgery via bronchoscopy suction channel. See text for details (reprinted from Ku et al. [110], with permission).

segments throughout the period of insufflation [110]. Distal oxygen insufflation, particularly at relatively high flow rates as described in this report, should never be applied blindly. As another option, we have successfully used HFJV during VATS procedures. In order for this technique to succeed, the lung has to be allowed to collapse away from the chest wall prior to the institution of HFJV and driving pressures have to be low enough to only cause partial lung inflation. As previously stated, however, with proper attention to adequate lung isolation, “open lung” ventilation and maintenance of a normal cardiac output, these interventions should rarely be necessary.

Lung de-recruitment in the ventilated lung is common, easily reversed with recruitment maneuvers and preventable with appropriate PEEP levels. Low mixed venous oxygen saturation secondary to low cardiac output is another frequent and easily treatable cause of desaturation. Pharmacological modulation with vasoconstrictors (almitrine, phenylephrine) to strengthen HPV in the operative lung and vasodilators (inhaled NO) to improve pulmonary vascular capacitance in the ventilated lung may be helpful in extreme cases.

Systemic Effects

Even though hypoxia has become less of an anesthetic issue during OLV, relative hypoxemia may have a significant impact on vital nonpulmonary organ function due to the ever-increasing rate of co-morbid conditions in thoracic patients. In addition to hypoxemia, release of inflammatory

cytokines and reactive oxygen metabolites may have yet unknown effects on organ function. A few recent studies have attempted to define the effects of OLV on organ function. More research is needed to delineate the end-organ effects of OLV.

A recent study by Mierdl et al. analyzed the impact of hypoxia during OLV on myocardial metabolism in patients with severe multi-vessel coronary artery disease. Patients underwent minimally invasive coronary artery bypass grafting via small lateral thoracotomy. In their study measurements of arterial and coronary sinus PO_2 , pH and lactate did not show any evidence of anaerobic metabolism, despite arterial PO_2 values between 50 and 70 mmHg during OLV. Additionally, no patient exhibited myocardial ischemia, which led the authors to conclude that OLV may be used in patients with multi-vessel coronary artery disease with an acceptable low risk of inducing anaerobic myocardial metabolism [111].

Neurocognitive dysfunction is a well-known complication of cardiac surgery, and has been shown to be associated with intraoperative episodes of cerebral oxygen desaturation. Standard pulse oximetry is insufficient to detect these events. Monitoring for, and treating cerebral desaturation events, may decrease the incidence of postoperative neurocognitive dysfunction [112, 113]. Tobias et al. investigated the incidence and risk factors for cerebral desaturation by monitoring cerebral oxygenation (rSO_2) using near infrared spectroscopy in patients who required OLV for thoracic surgery [114]. In 8 of 40 patients, prolonged decreases in rSO_2 to less than 75% of the baseline value were recorded for 25% or more of the

duration of OLV. These eight patients were older, weighed more and were more likely to be ASA III than the remainder of the patients. Since there was no significant difference in patient background or other monitoring values, the authors concluded that rSO_2 monitoring might be useful to detect cerebral desaturation and allow for early intervention in patients during OLV. Jugular bulb venous oxygen saturations during OLV were assessed in a study comparing sevoflurane- and propofol-based anesthesia in patients undergoing lung surgery [115]. The SjO_2 values were significantly higher in the sevoflurane group than in the propofol group, despite identical SaO_2 values. The lower SjO_2 values observed with propofol anesthesia may be explained by the fact that propofol reduces cerebral blood flow more than cerebral metabolic rate [116, 117].

Interestingly, cerebral oxygen desaturation also appears to be predictive of noncerebral postoperative complications. In a recent trial of 50 patients undergoing major thoracotomy with OLV, a minimal absolute regional cerebral oxygen saturation of less than 65% was found to be predictive of postoperative organ dysfunction based on the Sequential Organ Failure Assessment (SOFA) scoring system with an OR of 2.37 (95% CI 1.18–4.39, $P=0.043$) [118]. Cerebral tissue oxygenation depends on arterial oxygen content, oxygen delivery (cardiac output) and metabolic consumption and may therefore be a superior monitor to simple pulse oximetry.

Reactive oxygen metabolites are known to occur after re-expansion of the nonventilated lung. These metabolites may have deleterious effects on cellular function. Yulu et al. investigated the effects of OLV and re-expansion on the tissue damage of the liver and ileum in rats [119]. Plasma aspartate aminotransferase (AST), alanine aminotransferase (ALT), tissue MDA, and MPO activities in both tissues were significantly increased associated with OLV and re-expansion. Tissue damage and apoptotic index increased in rats with longer OLV duration, suggesting that OLV may cause tissue damage in the liver and ileum. These are some of the early indicators that OLV may indeed have effects beyond lung tissue; future research will help to delineate the significance of these findings.

Conclusion

The last decade has seen a shift in OLV research from studies investigating hypoxemia to various aspects of lung injury pathophysiology and prevention. Much has been learned about ventilation strategies that minimize lung injury. Evidence to date supports PLV based on reduction of surrogate markers, but more importantly now also indicates reduction of adverse outcomes. Ventilatory parameters have to be individualized for each patient's unique pulmonary mechanics, but should focus on an "open-lung" strategy. Hypoxemia is infrequent and should lead to a re-evaluation of ventilatory parameters. Routine algorithms for treatment of hypoxemia, as well as

advanced management techniques are available, such that prolonged hypoxia should be exceedingly rare. There are early indicators that OLV may impact systemic organ function, but future research is needed to address end-organ effects.

References

1. Brodsky JB. The evolution of thoracic anesthesia. *Thorac Surg Clin.* 2005;15(1):1–10.
2. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin.* 2008;26(2):241–72.
3. Zeldin RA, Normandin D, Landtwing D, Peters RM. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg.* 1984;87(3):359–65.
4. Licker M, Fauconnet P, Villiger Y, Tschoopp JM. Acute lung injury and outcomes after thoracic surgery. *Curr Opin Anesthesiol.* 2009;22(1):61–7.
5. Dulu A, Pastores SM, Park B, Riedel E, Rusch V, Halpern NA. Prevalence and mortality of acute lung injury and ARDS after lung resection. *Chest.* 2006;130(1):73–8.
6. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med.* 1994;149(3 Pt 1):818–24.
7. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97(6):1558–65.
8. Ruffini E, Parola A, Papalia E, et al. Frequency and mortality of acute lung injury and acute respiratory distress syndrome after pulmonary resection for bronchogenic carcinoma. *Eur J Cardiothorac Surg.* 2001;20(1):30–7.
9. Kutlu CA, Williams EA, Evans TW, Pastorino U, Goldstraw P. Acute lung injury and acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg.* 2000;69(2):376–80.
10. Alam N, Park BJ, Wilton A, et al. Incidence and risk factors for lung injury after lung cancer resection. *Ann Thorac Surg.* 2007;84(4):1085–91.
11. Tang SS, Redmond K, Griffiths M, Ladas G, Goldstraw P, Dusmet M. The mortality from acute respiratory distress syndrome after pulmonary resection is reducing: a 10-year single institutional experience. *Eur J Cardiothorac Surg.* 2008;34(4):898–902.
12. Jordan S, Mitchell JA, Quinlan GJ, Goldstraw P, Evans TW. The pathogenesis of lung injury following pulmonary resection. *Eur Respir J.* 2000;15(4):790–9.
13. Tremblay LN, Slutsky AS. Ventilator-induced lung injury: from the bench to the bedside. *Intensive Care Med.* 2006;32(1):24–33.
14. Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med.* 1998;338(6):347–54.
15. Schultz MJ, Haitsma JJ, Slutsky AS, Gajic O. What tidal volumes should be used in patients without acute lung injury? *Anesthesiology.* 2007;106(6):1226–31.
16. Putensen C, Wrigge H. Tidal volumes in patients with normal lungs: one for all or the less, the better? *Anesthesiology.* 2007;106(6):1085–7.
17. Padley SPG, Jordan SJ, Goldstraw P, Wells AU, Hansell DM. Asymmetric ARDS following pulmonary resection: CT findings initial observations. *Radiology.* 2002;223(2):468–73.

18. Yin K, Gribbin E, Emanuel S, et al. Histochemical alterations in one-lung ventilation. *J Surg Res.* 2007;137(1):16–20.
19. Kozian A, Schilling T, Fredén F, et al. One-lung ventilation induces hyperperfusion and alveolar damage in the ventilated lung: an experimental study. *Br J Anaesth.* 2008;100(4):549–59.
20. Funakoshi T, Ishibe Y, Okazaki N, et al. Effect of re-expansion after short-period lung collapse on pulmonary capillary permeability and proinflammatory cytokine gene expression in isolated rabbit lungs. *Br J Anaesth.* 2004;92(4):558–63.
21. Schilling T, Kozian A, Huth C, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. *Anesth Analg.* 2005;101(4):957–65.
22. Michelet P, D'Journo XB, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology.* 2006;105(5):911–9.
23. Sentürk M. New concepts of the management of one-lung ventilation. *Curr Opin Anaesthesiol.* 2006;19(1):1–4.
24. De Conno E, Steurer MP, Wittlinger M, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *Anesthesiology.* 2009;110(6):1316–26.
25. Giraud O, Molliex S, Rolland C, et al. Halogenated anesthetics reduce interleukin-1 β -induced cytokine secretion by rat alveolar type II cells in primary culture. *Anesthesiology.* 2003;98(1):74–81.
26. Schilling T, Kozian A, Kretschmar M, et al. Effects of propofol and desflurane anaesthesia on the alveolar inflammatory response to one-lung ventilation. *Br J Anaesth.* 2007;99(3):368–75.
27. Cohen E. Management of one-lung ventilation. *Anesthesiol Clin North America.* 2001;19(3):475–95.
28. Brodsky JB, Fitzmaurice B. Modern anesthetic techniques for thoracic operations. *World J Surg.* 2001;25(2):162–6.
29. Bendixen HH, Hedley-Whyte J, Laver MB. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. *N Engl J Med.* 1963;269:991–6.
30. Katz JA, Laverne RG, Fairley HB, Thomas AN. Pulmonary oxygen exchange during endobronchial anesthesia: effect of tidal volume and PEEP. *Anesthesiology.* 1982;56(3):164–71.
31. Flacke JW, Thompson DS, Read RC. Influence of tidal volume and pulmonary artery occlusion on arterial oxygenation during endobronchial anesthesia. *South Med J.* 1976;69(5):619–26.
32. van der Werff YD, van der Houwen HK, Heijmans PJ, et al. Postpneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest.* 1997;111(5):1278–84.
33. Fernández-Pérez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology.* 2006;105(1):14–8.
34. Neustein S. Association of high tidal volume with postpneumonectomy failure. *Anesthesiology.* 2007;106(4):875–6.
35. Jeon K, Yoon JW, Suh GY, et al. Risk factors for post-pneumonectomy acute lung injury/acute respiratory distress syndrome in primary lung cancer patients. *Anaesth Intensive Care.* 2009;37(1):14–9.
36. Gama de Abreu M, Heintz M, Heller A, Szechenyi R, Albrecht DM, Koch T. One-lung ventilation with high tidal volumes and zero positive end-expiratory pressure is injurious in the isolated rabbit lung model. *Anesth Analg.* 2003;96(1):220–8.
37. Kuzkov VV, Suborov EV, Kirov MY, et al. Extravascular lung water after pneumonectomy and one-lung ventilation in sheep. *Crit Care Med.* 2007;35(6):1550–9.
38. Chiumello D, Pristine G, Slutsky A. Mechanical ventilation affects local and systemic cytokines in an animal model of acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1999;160(1):109–16.
39. Cepkova M, Brady S, Sapru A, Matthay MA, Church G. Biological markers of lung injury before and after the institution of positive pressure ventilation in patients with acute lung injury. *Crit Care.* 2006;10(5):R126.
40. Parsons PE, Eisner MD, Thompson BT, et al. Lower tidal volume ventilation and plasma cytokine markers of inflammation in patients with acute lung injury. *Crit Care Med.* 2005;33(1):1–6.
41. Wrigge H, Uhlig U, Zinserling J, et al. The effects of different ventilatory settings on pulmonary and systemic inflammatory responses during major surgery. *Anesth Analg.* 2004;98(3):775–81.
42. Boyle NH, Pearce A, Hunter D, Owen WJ, Mason RC. Intraoperative scanning laser Doppler flowmetry in the assessment of gastric tube perfusion during esophageal resection. *J Am Coll Surg.* 1999;188(5):498–502.
43. Tusman G, Böhm SH, Suárez Sipmann F, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. *Anesth Analg.* 2004;98(6):1604–9.
44. Licker M, Diaper J, Villiger Y, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. *Crit Care.* 2009;13(2):R41.
45. Klingschedt C, Hedenstierna G, Baehrendtz S, Lundqvist H, Strandberg A, Tokics L, et al. Ventilation-perfusion relationships and atelectasis formation in the supine and lateral positions during conventional mechanical and differential ventilation. *Acta Anaesthesiol Scand.* 1990;34(6):421–9.
46. Ducros L, Moutafis M, Castelain MH, Liu N, Fischler M. Pulmonary air trapping during two-lung and one-lung ventilation. *J Cardiothorac Vasc Anesth.* 1999;13(1):35–9.
47. Slinger PD, Hickey DR. The interaction between applied PEEP and auto-PEEP during one-lung ventilation. *J Cardiothorac Vasc Anesth.* 1998;12(2):133–6.
48. Caramez MP, Borges JB, Tucci MR, et al. Paradoxical responses to positive end-expiratory pressure in patients with airway obstruction during controlled ventilation. *Crit Care Med.* 2005;33(7):1519–28.
49. Slinger PD, Kruger M, McRae K, Winton T. Relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung ventilation. *Anesthesiology.* 2001;95(5):1096–102.
50. Valenza F, Ronzoni G, Perrone L, et al. Positive end-expiratory pressure applied to the dependent lung during one-lung ventilation improves oxygenation and respiratory mechanics in patients with high FEV1. *Eur J Anaesthesiol.* 2004;21(12):938–43.
51. Ren Y, Peng ZL, Xue QS, Yu BW. The effect of timing of application of positive end-expiratory pressure on oxygenation during one-lung ventilation. *Anaesth Intensive Care.* 2008;36(4):544–8.
52. Bardoczky GI, d'Hollander AA, Cappello M, Yernault JC, et al. Interrupted expiratory flow on automatically constructed flow volume curves may determine the presence of intrinsic positive end-expiratory pressure during one-lung ventilation. *Anesth Analg.* 1998;86(4):880–4.
53. Misthos P, Katsaragakis S, Theodorou D, Milengos N, Skottis I. The degree of oxidative stress is associated with major adverse effects after lung resection: a prospective study. *Eur J Cardiothorac Surg.* 2006;29(4):591–5.

54. Douzinas EE, Kollias S, Tiniakos D, et al. Hypoxicemic reperfusion after 120 mins of intestinal ischemia attenuates the histopathologic and inflammatory response. *Crit Care Med.* 2004;32(11):2279–83.
55. Duggan M, Kavanagh BP. Atelectasis in the perioperative patient. *Curr Opin Anaesthesiol.* 2007;20(1):37–42.
56. Bardoczky GI, Szegedi LL, d'Hollander AA, Moures JM, De Francquen P, Yernault JC. Two-lung and one-lung ventilation in patients with chronic obstructive pulmonary disease: the effects of position and F(1O)2. *Anesth Analg.* 2000;90(1):35–41.
57. Ko R, McRae K, Darling G, et al. The use of air in the inspired gas mixture during two-lung ventilation delays lung collapse during one-lung ventilation. *Anesth Analg.* 2009;108(4):1092–6.
58. Kregenow DA, Rubenfeld GD, Hudson LD, Swenson ER. Hypercapnic acidosis and mortality in acute lung injury. *Crit Care Med.* 2006;34(1):1–7.
59. Lang CJ, Barnett EK, Doyle IR. Stretch and CO2 modulate the inflammatory response of alveolar macrophages through independent changes in metabolic activity. *Cytokine.* 2006;33(6):346–51.
60. Sticher J, Muller M, Scholz S, Schindler E, Hempelmann G. Controlled hypercapnia during one-lung ventilation in patients undergoing pulmonary resection. *Acta Anaesthesiol Scand.* 2001;45(7):842–7.
61. Zollinger A, Zaugg M, Weder W, et al. Video-assisted thoracoscopic volume reduction surgery in patients with diffuse pulmonary emphysema: gas exchange and anesthesiological management. *Anesth Analg.* 1997;84(4):845–51.
62. Morisaki H, Serita R, Innami Y, Kotake Y, Takeda J. Permissive hypercapnia during thoracic anaesthesia. *Acta Anaesthesiol Scand.* 1999;43(8):845–9.
63. Balanos GM, Talbot NP, Dorrington KL, Robbins PA. Human pulmonary vascular response to 4 h of hypercapnia and hypocapnia measured using Doppler echocardiography. *J Appl Physiol.* 2003;94(4):1543–51.
64. Robinson RJ, Shennib H, Noirclerc M. Slow-rate, high-pressure ventilation: a method of management of difficult transplant recipients during sequential double lung transplantation for cystic fibrosis. *J Heart Lung Transplant.* 1994;13(5):779–84.
65. Szegedi LL, Barvais L, Sokolow Y, Yernault JC, D'Hollander AA. Intrinsic positive end-expiratory pressure during one-lung ventilation of patients with pulmonary hyperinflation. Influence of low respiratory rate with unchanged minute volume. *Br J Anaesth.* 2002;88(1):56–60.
66. Slinger PD, Lesiuk L. Flow resistances of disposable double-lumen, single-lumen, and univent tubes. *J Cardiothorac Vasc Anesth.* 1998;12(2):142–4.
67. Szegedi LL, Bardoczky GI, Engelman EE, D'Hollander AA. Airway pressure changes during one-lung ventilation. *Anesth Analg.* 1997;84(5):1034–7.
68. Fernández-Pérez ER, Sprung J, Afessa B, et al. Intraoperative ventilator settings and acute lung injury after elective surgery: a nested case control study. *Thorax.* 2009;64(2):121–7.
69. Nichols D, Haranath S. Pressure control ventilation. *Crit Care Clin.* 2007;23(2):183–99.
70. Tu rul M, Camci E, Karadeniz H, Sentürk M, Pembeci K, Akpir K. Comparison of volume-controlled with pressure-controlled ventilation during one-lung anaesthesia. *Br J Anaesth.* 1997;79(3):306–10.
71. Sentürk NM, Dilek A, Camci E, et al. Effects of positive end-expiratory pressure on ventilatory and oxygenation parameters during pressure-controlled one-lung ventilation. *J Cardiothorac Vasc Anesth.* 2005;19(1):71–5.
72. Unzueta MC, Casas JI, Moral MV. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation for thoracic surgery. *Anesth Analg.* 2007;104(5):1029–33.
73. Leong LM, Chatterjee S, Gao F. The effect of positive end-expiratory pressure on the respiratory profile during one-lung ventilation for thoracotomy. *Anaesthesia.* 2007;62(1):23–6.
74. Choi YS, Shim JK, Na S, Hong SB, Hong YW, Oh YJ. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation in the prone position for robot-assisted esophagectomy. *Surg Endosc.* 2009;23(10):2286–91.
75. Heimberg C, Winterhalter M, Strüber M, Piepenbrock S, Bund M. Pressure-controlled versus volume-controlled one-lung ventilation for MIDCAB. *Thorac Cardiovasc Surg.* 2006;54(8):516–20.
76. Cruz Pardos P, Garutti I, Piñeiro P, Olmedilla L, de la Gala F. Effects of ventilatory mode during one-lung ventilation on intraoperative and postoperative arterial oxygenation in thoracic surgery. *J Cardiothorac Vasc Anesth.* 2009;23(6):770–4.
77. Ihra G, Gockner G, Kashanipour A, Aloy A. High-frequency jet ventilation in European and North American institutions: developments and clinical practice. *Eur J Anaesthesiol.* 2000;17(7):418–30.
78. Abe K, Oka J, Takahashi H, Funatsu T, Fukuda H, Miyamoto Y. Effect of high-frequency jet ventilation on oxygenation during one-lung ventilation in patients undergoing thoracic aneurysm surgery. *J Anesth.* 2006;20(1):1–5.
79. Knutgen D, Zeidler D, Vorweg M, Doebe M. Unilateral high-frequency jet ventilation supporting one-lung ventilation during thoracic surgical procedures. *Anaesthesist.* 2001;50(8):585–9.
80. Misolek H, Knapik P, Swanevelder J, Wyatt R, Misolek M. Comparison of double-lung jet ventilation and one-lung ventilation for thoracotomy. *Eur J Anaesthesiol.* 2008;25(1):15–21.
81. Buise M, van Bommel J, van Genderen M, Tilanus H, van Zundert A, Gommers D. Two-lung high-frequency jet ventilation as an alternative ventilation technique during transthoracic esophagectomy. *J Cardiothorac Vasc Anesth.* 2009;23(4):509–12.
82. Lentz CW, Peterson HD. Smoke inhalation is a multilevel insult to the pulmonary system. *Curr Opin Pulm Med.* 1997;3(3):221–6.
83. Reper P, Dankaert R, van Hille F, van Laeke P, Duinslaeger L, Vanderkelen A. The usefulness of combined high-frequency percussive ventilation during acute respiratory failure after smoke inhalation. *Burns.* 1998;24(1):34–8.
84. Velmahos GC, Chan LS, Tatevossian R, et al. High-frequency percussive ventilation improves oxygenation in patients with ARDS. *Chest.* 1999;116(2):440–6.
85. Lucangelo U, Antonaglia V, Zin WA, et al. High-frequency percussive ventilation improves perioperatively clinical evolution in pulmonary resection. *Crit Care Med.* 2009;37(5):1663–9.
86. Duggan M, McCaul CL, McNamara PJ, Engelberts D, Ackerley C, Kavanagh BP. Atelectasis causes vascular leak and lethal right ventricular failure in uninjured rat lungs. *Am J Respir Crit Care Med.* 2003;167(12):1633–40.
87. Cinnella G, Grasso S, Natale C, et al. Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. *Acta Anaesthesiol Scand.* 2008;52(6):766–75.
88. Michelet P, Roch A, Brousse D, et al. Effects of PEEP on oxygenation and respiratory mechanics during one-lung ventilation. *Br J Anaesth.* 2005;95(2):267–73.

89. Vieillard-Baron A, Charron C, Jardin F. Lung "recruitment" or lung overinflation maneuvers? *Intensive Care Med.* 2006; 32(1):177–8.
90. Garutti I, Martinez G, Cruz P, Piñeiro P, Olmedilla L, de la Gala F. The impact of lung recruitment on hemodynamics during one-lung ventilation. *J Cardiothorac Vasc Anesth.* 2009;23(4): 506–8.
91. Koh WJ, Suh GY, Han J, et al. Recruitment maneuvers attenuate repeated derecruitment-associated lung injury. *Crit Care Med.* 2005;33(5):1070–6.
92. Suh GY, Koh Y, Chung MP, et al. Repeated derecruitments accentuate lung injury during mechanical ventilation. *Crit Care Med.* 2002;30(8):1848–53.
93. Farias LL, Faffe DS, Xisto DG, et al. Positive end-expiratory pressure prevents lung mechanical stress caused by recruitment/derecruitment. *J Appl Physiol.* 2005;98(1):53–61.
94. Halbertsma FJ, Vanekern M, Pickkers P, Neeleman C, Scheffer GJ, van der Hoeven JG. A single recruitment maneuver in ventilated critically ill children can translocate pulmonary cytokines into the circulation. *J Crit Care.* 2010;25(1):10–5.
95. Meade MO, Cook DJ, Griffith LE, et al. A study of the physiologic responses to a lung recruitment maneuver in acute lung injury and acute respiratory distress syndrome. *Respir Care.* 2008;53(11):1441–9.
96. Sivrikoz MC, Tuncozgur B, Cekmen M, et al. The role of tissue reperfusion in the re-expansion injury of the lungs. *Eur J Cardiothorac Surg.* 2002;22(5):721–7.
97. Ojima H, Kuwano H, Kato H, et al. Relationship between cytokine response and temporary ventilation during one-lung ventilation in esophagectomy. *Hepatogastroenterology.* 2007;54(73):111–5.
98. Hansen LK, Koefoed-Nielsen J, Nielsen J, Larsson A. Are selective lung recruitment maneuvers hemodynamically safe in severe hypovolemia? An experimental study in hypovolemic pigs with lobar collapse. *Anesth Analg.* 2007;105(3): 729–34.
99. Mahfood S, Hix WR, Aaron BL, Blaes P, Watson DC. Re-expansion pulmonary edema. *Ann Thorac Surg.* 1988;45(3): 340–5.
100. Tekinbas C, Ulusoy H, Yulug E, et al. One-lung ventilation: for how long? *J Thorac Cardiovasc Surg.* 2007;134(2):405–10.
101. Hurford WE, Kolker AC, Strauss HW. The use of ventilation/perfusion lung scans to predict oxygenation during one-lung anesthesia. *Anesthesiology.* 1987;67(5):841–4.
102. Slinger P, Suissa S, Adam J, Triolet W. Predicting arterial oxygenation during one-lung ventilation with continuous positive airway pressure to the nonventilated lung. *J Cardiothorac Anesth.* 1990;4(4):436–40.
103. Yamamoto Y, Watanabe S, Kano T. Gradient of bronchial end-tidal CO₂ during two-lung ventilation in lateral decubitus position is predictive of oxygenation disorder during subsequent one-lung ventilation. *J Anesth.* 2009;23(2):192–7.
104. Fukuoka N, Iida H, Akamatsu S, Nagase K, Iwata H, Dohi S. The association between the initial end-tidal carbon dioxide difference and the lowest arterial oxygen tension value obtained during one-lung anesthesia with propofol or sevoflurane. *J Cardiothorac Vasc Anesth.* 2009;23(6):775–9.
105. Hurford WE, Alfillé PH. A quality improvement study of the placement and complications of double-lumen endobronchial tubes. *J Cardiothorac Vasc Anesth.* 1993;7(5):517–20.
106. Brodsky JB, Lemmens HJ. Left double-lumen tubes: clinical experience with 1170 patients. *J Cardiothorac Vasc Anesth.* 2003;17(3):289–98.
107. Ehrenfeld JM, Walsh JL, Sandberg WS. Right- and left-sided Mallinckrodt double-lumen tubes have identical clinical performance. *Anesth Analg.* 2008;106(6):1847–52.
108. Baraka AS, Taha SK, Yaacoub CI. Alarming hypoxemia during one-lung ventilation in a patient with respiratory bronchiolitis-associated interstitial lung disease. *Can J Anaesth.* 2003;50(4):411–4.
109. Russell WJ. Intermittent positive airway pressure to manage hypoxia during one-lung anaesthesia. *Anaesth Intensive Care.* 2009;37(3):432–4.
110. Ku CM, Slinger P, Waddell TK. A novel method of treating hypoxemia during one-lung ventilation for thoracoscopic surgery. *J Cardiothorac Vasc Anesth.* 2009;23(6):850–2.
111. Mierdl S, Meininger D, Dogan S, et al. Does poor oxygenation during one-lung ventilation impair aerobic myocardial metabolism in patients with symptomatic coronary artery disease? *Interact Cardiovasc Thorac Surg.* 2007;6(2):209–13.
112. Casati A, Fanelli G, Pietropaoli P, et al. Continuous monitoring of cerebral oxygen saturation in elderly patients undergoing major abdominal surgery minimizes brain exposure to potential hypoxia. *Anesth Analg.* 2005;101(3):740–7.
113. Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg.* 2007;104(1):51–8.
114. Tobias JD, Johnson GA, Rehman S, Fisher R, Caron N. Cerebral oxygenation monitoring using near infrared spectroscopy during one-lung ventilation in adults. *J Minim Access Surg.* 2008;4(4):104–7.
115. Iwata M, Inoue S, Kawaguchi M, et al. Jugular bulb venous oxygen saturation during one-lung ventilation under sevoflurane- or propofol-based anesthesia for lung surgery. *J Cardiothorac Vasc Anesth.* 2008;22(1):71–6.
116. Van Hemelrijck J, Fitch W, Mattheussen M, Van Aken H, Pleits C, Lauwers T. Effect of propofol on cerebral circulation and autoregulation in the baboon. *Anesth Analg.* 1990;71(1): 49–54.
117. Vandesteene A, Tremont V, Engelman E, et al. Effect of propofol on cerebral blood flow and metabolism in man. *Anaesthesia.* 1988;43(Suppl):42–3.
118. Kazan R, Bracco D, Hemmerling TM. Reduced cerebral oxygen saturation measured by absolute cerebral oximetry during thoracic surgery correlates with postoperative complications. *Br J Anaesth.* 2009;103(6):811–6.
119. Yulu E, Tekinbas C, Ulusoy H, et al. The effects of oxidative stress on the liver and ileum in rats caused by one-lung ventilation. *J Surg Res.* 2007;139(2):253–60.
120. Kozian A, et al. Lung computed tomography density distribution in a porcine model of one-lung ventilation. *Br J Anaesth.* 2009;102(4):551–60.
121. Dueck R, et al. A pilot study of expiratory flow limitation and lung volume reduction surgery. *Chest.* 1999;116:1762–71.

Nonrespiratory Functions of the Lung

Lauren Yeazell and Keith Littlewood

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Key Points

- Pulmonary endothelial cells metabolize endogenous substances and xenobiotics via ecto-enzymes on their luminal surface and caveolae or enzyme systems within their cytosol.
- Pulmonary metabolism results in the activation of several endogenous substances and some medications of importance to the anesthesiologist.
- Pulmonary uptake is often not associated with metabolism, but still markedly affects pharmacokinetics by initially attenuating peak concentrations and then returning unchanged substance to the circulation.
- The lung's ability to serve as a vascular reservoir is directly related to the capacitance of the pulmonary vessels.
- The lung serves as a physical filter but this function may be compromised with high cardiac output and in several disease states.
- The respiratory epithelium's functions include humidification and trapping of particles and pathogens.
- The airway surface film has antimicrobial capacity beyond its mechanical removal of debris from the airway.

Introduction

For nearly two millennia of Western medicine, the lungs were thought to primarily protect the heart from overheating by exhaling warm air and from direct injury both by their position and cushioning structure. These views are ascribed to the teachings of Galen and, to some extent, Aristotle [1, 2]. Traditional Chinese medicine emphasized the interconnectedness of the organ groupings of the five phases, but within this construct the Lung was seen as a minister to the emperor Heart

and in partnership with the bowel to have the responsibility of maintaining the boundary of body and outside world. In the thirteenth century, Ibn-an-Nafis of Cairo described the purification of blood by mixing with air in the lungs in one of the earliest known descriptions of gas exchange [3].

Over the last several centuries, however, the biochemistry and physiology of respiration have become essentially synonymous with the lungs. From the work of pioneers such as Boyle, Lower, Priestly, Haldane, and others, most clinicians now think of the lung first and foremost as an organ of gas exchange. In more recent years, other important roles of the lung have emerged, roles that are often in keeping with the concepts of our medical heritages.

In this sense, then, we now return to historic views of the lung as protector and modulator. Specifically, nonrespiratory functions of the lung including its metabolic processes, endocrine role, mechanical filtration of venous blood, warming of inspired gasses, and protection against inhaled pathogens and toxins are discussed. Focused aspects of organ structure and cellular function are reviewed as required by this discussion.

Uptake and Metabolism Within the Lung

The lungs are particularly suited for critical metabolic activities. They continuously receive essentially the entire cardiac output and their vascular area, depending upon the degree of recruitment, is an enormous $70\text{--}100\text{ m}^2$. Further, the lungs contain nearly half of the body's endothelium [4] and have an extraordinarily high perfusion of $14\text{ mL/min g tissue}$ (as opposed to the next-highest renal perfusion of 4 mL/min g tissue). Thus, there is ample blood–endothelial interface for surface enzyme activity as well as uptake and secretion. The

largest population of cells involved in pulmonary metabolism of blood-borne substances is, as might be expected, the pulmonary endothelium. Consistent with high metabolic activity, endothelial cells typically have both extensive cytoplasmic vesicles and prominent caveolae. The caveolae are tiny membrane invaginations and near-membrane vesicles similar to those found elsewhere in the body, measuring 50–100 nm, associated with caveolin proteins, and derived from lipid rafts within the membrane. The predominant activities of these caveolae, thought to include endocytosis [5] and signal transduction, have not been fully delineated, and may be pleiotropic [6]. The endothelial cells structurally have large luminal projections and invaginations, providing an even greater interface area at the microscopic level.

Metabolism by the endothelial cell occurs either on the surface of the cell via enzymes associated with the membrane (“ecto-enzymes”) or by cytosolic processing after the substances are taken up by the cell. Some surface enzymes are distributed along the luminal membrane [7], while others are associated exclusively with the caveolae [8]. Figure 7.1 schematically depicts these processes with example substances and pathways. Metabolism may be further divided into exogenous vs. endogenous substances as well as deactivated vs.

activated products. Regardless of these considerations, it should be remembered that intensive investigation of pulmonary metabolism has developed only over the last several decades [9]. Much remains to be discovered and conflicting data exist for drugs as central to clinical anesthesiology as propofol [10, 11].

The literature’s terminology of pulmonary metabolism can also be confusing and sometimes inconsistent. The careful reader must sometimes deduce the actual processes described and investigated through context. In general, “pulmonary uptake” (and, often, “extraction”) is simply used to describe transfer from blood to lung. It does not indicate whether the substance of interest is subsequently metabolized or returned back into the blood (with or without alteration). “First-pass” uptake is used to describe the amount of substance removed from the blood on the first cycle through the lungs, although data from techniques such as tissue slices have been used to infer this behavior. “Extraction” is also sometimes used synonymously with first-pass uptake. “Clearance” may be used to describe a substance undergoing actual elimination, either in terms similar to renal clearance as volume of blood from which the substance would be completely removed (mL/min or mL/kg min), or as a comparison of pulmonary arterial

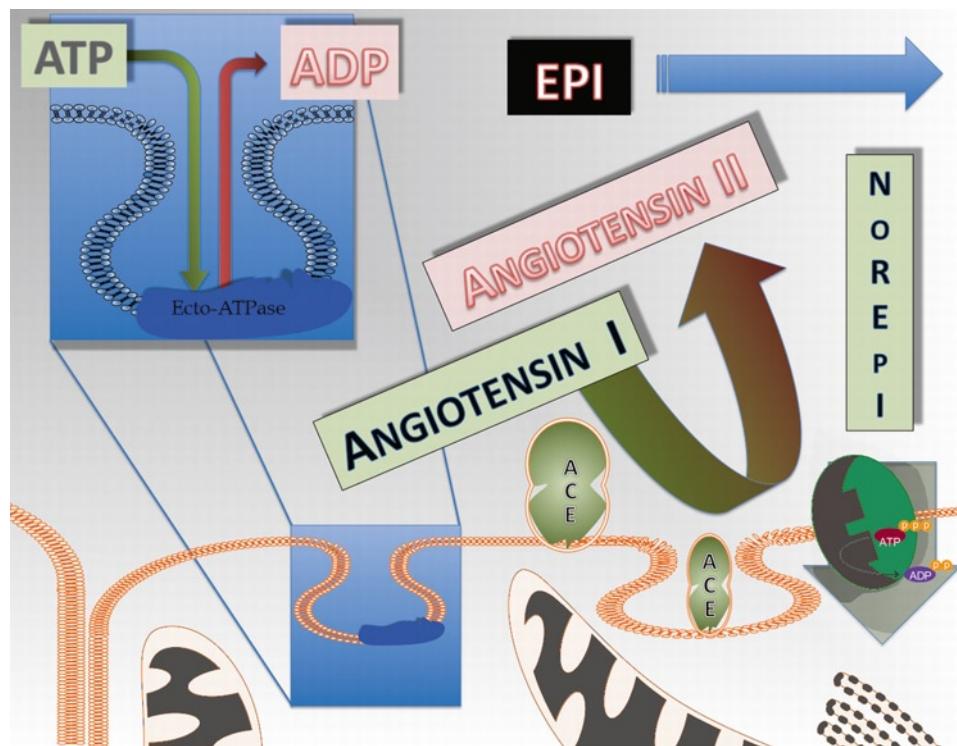


FIG. 7.1. Schematic examples of pulmonary endothelial metabolism. Surface enzymes may be restricted to the caveolae (Ecto-ATPase in the inset above is an example), or present on both the luminal surface and caveola (e.g., angiotensin converting enzyme [ACE]). Another characteristic of pulmonary endothelium is selective uptake, here exemplified by the ATP-dependent uptake of norepinehrine (NOREPI), while epinephrine (EPI) is not taken up. See text for details.

concentration vs. systemic arterial concentration. Terms used for isolated lung studies include “accumulation” (percentage of substance retained in the lungs after equilibrium) and “persistence” (percentage of substance retained after washout).

It is beyond the scope of this discussion to fully detail the experimental methods used in the investigation of pulmonary metabolism, but the challenges of investigation and data interpretation merit at least mention. As implied above, lung metabolism has been investigated *in vitro* and *in vivo*. *In vitro* techniques include the use of cellular fractionates, tissue homogenates, and tissue slices. Recent advances in uniform preparation and cryoprotection have made tissue slices an attractive, more cost-efficient option [12] despite concerns regarding the impact of processing on enzyme behavior. They have a particular advantage in lung research because they include all cell types. The isolated and perfused animal lung model represents the next level of fidelity. The lung can remain within the animal or be explanted and the uses of various perfusion managements (e.g., nonpulsatile vs. pulsatile, blood vs. crystalloid, and one-pass vs. recirculation) have been described with little standardization. Further, various investigators commonly subject the lung to no inflation, constant airway pressure, or positive pressure ventilation. The impact of these differences in ventilation on resultant data is unknown. In the next level of modeling, in intact animals and human subjects, the pulmonary uptake is typically assessed by measurements of the difference between pulmonary arterial and pulmonary venous (animals) or systemic arterial (human) concentrations of the substance in question, typically after a controlled bolus and/or infusion when possible. These invasive requirements do not lend themselves to large volunteer studies. Most human subjects are, in fact, critically ill and/or undergoing complex procedures. This variation in disease and treatment may produce data that in turn has great variance [13]. Conversely, inclusion criteria rigorous enough to provide consistent results produce a patient population in which the results are of limited general applicability [14]. A variation of the method just described is the double indicator-dilution technique [15]. In this technique, the substance of interest and a substance with no (or known) pulmonary uptake are injected, typically into the right atrium. Samples are then taken from a systemic artery, with the known substance serving as the control to which the investigated substance's concentration curve is compared. This technique is more practical in terms of decreased frequency of sampling, and somewhat decreased invasiveness.

It is important to reemphasize that the lung has a pronounced impact on the blood concentration of substances even when it does not ultimately break them down or secrete them. This is because of the simple uptake and retention of substances, often followed by release back into the blood. This “capacitor effect” [16] of the lungs in which any rapid rise or fall in concentration is attenuated will be revisited in the discussion below regarding local anesthetic toxicity.

TABLE 7.1. The lung and medications of interest to anesthesiologists.

Drug class	Impact of passage through the pulmonary circulation	
	Minimal or none	First-pass uptake and/or metabolism
<i>Hypnotics</i>		Thiopental + Ketamine ++ Propofol ++ Diazepam ++
<i>Benzodiazepines</i>		
<i>Nondepolarizing muscle relaxants</i>	Rocuronium Vecuronium Rapacuronium d-tubocurarine	
<i>Opiates</i>	Morphine	Fentanyl ++ Sufentanil + Alfentanil ± Norepinephrine +
<i>Catecholamines</i>	Dopamine Epinephrine Isoproterenol	
<i>Local anesthetics</i>		Bupivacaine + Lidocaine ++

With these limitations in mind, we shall first review the current understanding of drug metabolism with focus on medications of particular interest to the anesthesiologist, and then look at metabolism of endogenous substances. Endogenously produced substances such as catecholamines will be included in the latter discussion, even though they are also administered therapeutically and duplicated in the summary of medications (Table 7.1).

Drugs

The cytochrome P-450 monooxygenase enzyme systems are the most studied metabolic pathways for medications. The lungs have been found to have substantial concentrations of P-450 isoenzymes, particularly within type II pneumocytes, Clara cells, and endothelial cells [17]. This implies that the lung has the capacity for drug metabolism via its P-450 systems. While P-450 and other enzyme systems have long been known to exist in the human lung (Table 7.2), the actual activity of lung enzymes ranges from negligible to 33% of that of the liver [18]. The difference between organ enzyme activity of different species is large (lung to liver activity varying from a few percent to 111%) and mandates caution when interpreting animal data [19].

Opioids

Fentanyl has been shown to have a markedly variable first-pass uptake up to 90% in humans [20]. The same investigators found that significant amounts of fentanyl then returned from the lungs into the blood with a biphasic pattern, equilibrating after about a minute in the fast phase and nearly 25 min for the slow phase. The uptake of fentanyl is higher than expected

TABLE 7.2. Enzyme systems of the lung [86].

Cytochrome P-450 oxygenase
Sulphotransferase
Nitro reductase
<i>N</i> -Methyltransferase
Glutathione- <i>S</i> -epoxide transferase
Glutathione- <i>S</i> -aryl transferase
Glucuronyl transferase
Epoxide hydrolase
Amine oxidase

even for this basic and lipophilic drug. In fact, active uptake of fentanyl has been demonstrated in human lung endothelial cells [21].

The study of alfentanil has led to widely variant first-pass uptake data. Uptakes of 67% have been reported [20], as have (more commonly) uptakes of approximately 10% [22]. These studies both included other medications (sufentanil and morphine in one study and fentanyl in the other) that were found to behave similarly to accepted data for those drugs. This makes the discrepancy for alfentanil behavior particularly hard to interpret.

Sufentanil demonstrates uptake that is a little more than half that of fentanyl. A study in which patients had received alfentanil for induction followed by a sufentanil infusion of 50 µg/min for 10 min showed sufentanil first-pass uptake of about 50% with a 20-min retention of about 20% [23]. The investigators incidentally noted that smokers had a statistically higher retention of the infused dose.

Early work with morphine in the perfused rabbit lung model showed about 30% first-pass uptake [24]. Interestingly, subsequent work in intact animals and in patients has found much lower uptake of about 10% [22, 25], including postoperative bolus and infusion [26]. Metabolism has generally been found to be negligible.

Muscle Relaxants

There is a paucity of data on pulmonary pharmacokinetics of muscle relaxants. This may be because the agents studied, including vecuronium, rocuronium, d-tubocurarine, rapacuronium, and Org 7,617 demonstrated no first-pass uptake or metabolism in the intact porcine model [27]. This would appear to have generated little enthusiasm for further investigation of this class of drugs.

Local Anesthetics

Lidocaine has a long history of investigation in terms of pulmonary uptake and metabolism. The general consistencies across species include a first-pass uptake of approximately 50% with significant retention at 10 min [28–30]. The uptake of lidocaine has also been examined in a variety of physiological circumstances. Under extremes of metabolic acidosis and alkalosis [29], lidocaine demonstrates increased uptake

with higher blood pH. It is postulated that this finding is the consequence of increased drug lipophilicity, since, in a less acidic environment, more of the drug is in its nonionized form. Under extremes of FiO_2 in *in vivo* isolated lobes of dogs under nitrous oxide and halothane anesthesia, there were no differences demonstrated in lidocaine uptake [31]. Of interest, the prolonged retention in all groups was less than that commonly reported in other studies, raising the issue of the effects of this particular model on uptake.

Bupivacaine has been investigated less extensively than lidocaine and with less consistent results. In most animal species, peak extraction has been reported as high with variable first-pass retention between species and methodology [32–34]. In humans, however, the effective first-pass extraction appears to be lower when studied by epidural dosing [35, 36]. As in the case of lidocaine, the pulmonary pharmacokinetics of bupivacaine have been investigated in acidosis. In a rabbit model, animals with a pH of 7.0–7.1 demonstrated decreased maximum pulmonary extraction as a group [37] with resultant higher peak systemic concentrations of drugs.

Two recent areas of interest in the practice of clinical anesthesia are intimately linked with the pulmonary uptake of local anesthetics. The first is the relative safety of levobupivacaine and ropivacaine in comparison to bupivacaine. These drugs have, in fact, been the subject of several investigations. Early animal studies suggested decreased toxicity of these newer preparations [38, 39]. The discussion continues, however, with more recent work regarding the pulmonary uptake of these drugs. In rabbits, for example, the uptake of levobupivacaine is higher than ropivacaine with resultant lower systemic blood concentrations of levobupivacaine [40]. The authors thus caution that the lower absolute toxicity of ropivacaine may be tempered by the lung's greater attenuation of peak levobupivacaine levels in inadvertent intravenous injections. A recent review of the pharmacodynamics and pharmacokinetics of local anesthetics [41] focuses on the challenges of comparing toxicities in clinical practice [42–44]. Animal models, with the limitations already discussed amongst many more [45], must be utilized since clinical toxicity is an uncontrolled, rare, and dangerous event [46]. Other questions are raised by the relative central nervous system and cardiovascular toxicity between drugs and study variation in drug administration and measurement. The inconsistencies in the data of pulmonary uptake are thus one of many challenges in understanding the clinical toxicities of local anesthetics.

A second, related, area of great contemporary interest is the treatment of local anesthetic toxicity with lipid emulsion [47, 48]. A recent case report, in particular, is germane to the discussion of pulmonary uptake [49]. Briefly, a patient undergoing brachial plexus block with bupivacaine demonstrated evidence of toxicity by progressive symptomatology, seizures, widening QRS tachycardia, and asystole. Successful emulsified lipid "rescue" was followed nearly an hour later by recurrence of episodic ventricular tachycardia. The authors believe that this represented the first reported recurrence

of toxic bupivacaine levels after lipid treatment. Several possible causes were postulated for this phenomenon, including postresuscitation hepatic dysfunction, reversal of generalized peripheral ion-trapping of bupivacaine, and, appropriately, release of bupivacaine from the pulmonary vasculature. It seems that the issue of pulmonary uptake and release of local anesthetics must be considered in the treatment of suspected local anesthetic toxicity with emulsified lipid.

Hypnotics

There are limited, and sometimes dated, data regarding the pulmonary metabolism of intravenous induction agents. Thiopental has been found to have nearly 15% first-pass uptake in humans [50] with little or no metabolism. Ketamine shows marked species variation in its metabolism. In rabbit homogenate, the eventual complete disappearance of ketamine with only half being metabolized to norketamine implies the production of other metabolite(s) [51]. Lung tissue homogenate was more quickly saturated than liver tissue. As previously mentioned, the applicability of this homogenate data to intact animals, and certainly to patients, is unknown. In dogs under halothane anesthesia, the pulmonary uptake of ketamine was found to be slightly less than 10% without subsequent metabolism [52]. Human data are lacking.

The clarification of propofol uptake and metabolism by the lungs has taken many turns. One of the earliest studies in sheep with propofol administered as the sole medication demonstrated an apparent steady-state pulmonary clearance of 1.21 L/min [53] with negligible drug accumulation in the lung tissue while a later study in sheep demonstrated a similar 1.14 L/min pulmonary clearance [54]. Other early work found that propofol uptake in cats was nearly 60% but this uptake was particularly decreased in the presence of halothane or fentanyl [55]. Microsomal fractions from rat, rabbit, and human lung showed no glucuronidation of propofol [56]. Turning to data from human clinical studies, most recent work shows about 30% first-pass uptake and negligible metabolism of propofol by the lungs [11, 57]. It is interesting that a recently developed model of propofol pharmacodynamics and pharmacokinetics [58] has produced a very good fit with data from human studies [59, 60]. In this work, the lung is modeled as three tanks in series with the full cardiac output sequentially flowing to each, a model previously proven effective [61] in simulating the behavior of markers indocyanine green and antipyrine as well as the narcotic alfentanil.

Pulmonary Handling of Endogenous Substances

Angiotensin Converting Enzyme

This section will discuss the activity of angiotensin-converting enzyme (ACE) and two important substrates, angiotensin I and bradykinin. The lung plays a critical role in the renin–angiotensin system because of the pulmonary endothelium's

high concentration of ACE. When the kidney responds to changes in physiologic parameters such as vascular volume, blood pressure, and adrenergic stimulation by the cleaving of prorenin, the resultant renin catalyzes the formation of angiotensin I from angiotensinogen. It is ACE that then converts angiotensin I to the critically important vasoconstrictor, angiotensin II. Although ACE can be found on vascular endothelium throughout the body as well as in the plasma, the pulmonary endothelium has an abundance of ACE as a surface or ecto-enzyme on the vascular membrane [62, 63], including the caveolae (Figs. 7.1 and 7.2). The newly formed angiotensin II is not, in health, taken up or further metabolized by the endothelial cell, but rather immediately returns to the blood. Clinically, ACE inhibitors have been useful drugs in the management of systemic hypertension. As will be discussed below, the effects of these drugs are not limited simply to decreased levels of angiotensin II.

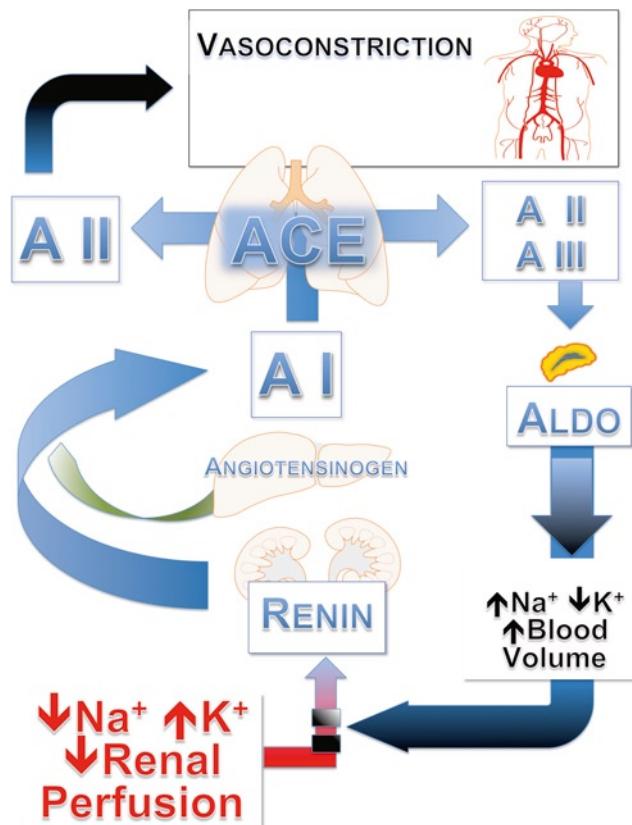


FIG. 7.2. An example of the lung's central role in the body's endocrine processes, in this case the renin–angiotensin–aldosterone axis. In response to sodium, potassium, and renal perfusion changes, renin is secreted by the kidneys. Renin cleaves angiotensinogen (renin substrate) from the liver to form angiotensin I (AI). The lung then converts AI to AII through the action predominately of endothelium-associated angiotensin-converting enzyme (ACE). AII causes vasoconstriction and is involved in stimulation of aldosterone (ALDO) secretion by the adrenal gland, resulting in retention of sodium and volume by the kidney.

Bradykinin is a nine amino-acid peptide produced in multiple sites throughout the body from kininogen through the action of plasma kallikrein. It is in turn metabolized by several peptidases. Pertinent to this discussion, bradykinin is degraded by ACE and, in fact, more than 90% of bradykinin is eliminated on first-pass through the lungs [64]. Bradykinin's effects are wide-ranging, including antithrombotic and profibrinolytic activity in the coagulation system, as well as modulation of nitric oxide and prostacyclin release. Specific to the lung, bradykinin was shown some time ago to have vasodilating effects on normal pulmonary vessels but to be vasoconstrictive when the pulmonary endothelium was destroyed in animal models [65, 66]. Bradykinin has also been long described as a bronchconstrictor [67, 68] and is still considered a prototypical bronchoconstricting substance [69]. The complexities of the kallikrein–kinin system's effect on endothelial cells, the myocardium, and vascular smooth muscle and its role in phenomena of cardiovascular injury is beyond the scope of this discussion, and the interested reader is referred to extensive reviews elsewhere [60, 70].

ACE is probably best known to clinicians through the drugs that block its activity, and, in fact, ACE inhibitors remain one of the most commonly prescribed group of drugs in the United States [71]. They are effective antihypertensive medications and have been shown to decrease the incidence of congestive heart failure after myocardial infarction [70]. It is now believed that some side effects of ACE inhibitors, such as angioedema and cough, and some of the beneficial impact, such as decreased myocardial infarctions and improved renal function, involve modification of bradykinin metabolism [60].

Biogenic Amines

Histamine, serotonin (5-hydroxytryptamine or 5-HT), and the three naturally occurring catecholamines dopamine, norepinephrine, and epinephrine comprise the group commonly termed biogenic amines. Studies looking into the uptake and metabolism of serotonin by the pulmonary circulation were amongst the earliest investigations of pulmonary pharmacokinetics [9, 72]. Subsequent work has made the behavior of this compound amongst the best understood in terms of pulmonary uptake and metabolism.

5-HT is produced predominately by the gastrointestinal tract's chromaffin cells. Ingested tryptophan undergoes a two-step conversion first by tryptophan-5-hydroxylase and then by L-amino acid decarboxylase to serotonin. Mast cells and neuroendocrine cells in the lung are also capable of producing serotonin by uptake of tryptophan along the same enzymatic pathway. However, the lung normally contributes minimally to systemic 5-HT production because of lesser tryptophan availability and much slower reaction rates [73]. Once released from the gastrointestinal tract, there is avid uptake of 5-HT, particularly by nerve endings and platelets. These cells do not metabolize 5-HT to any great extent. The remainder of 5-HT is extracted by the lung and, to a lesser degree, the liver.

In the case of these organs, the 5-HT is metabolized to 5-hydroxyindoleacetic acid (5-HIAA) by cytosolic monoamine oxidase and aldehyde dehydrogenase. 5-HIAA is, of course, a clinically useful marker of carcinoid syndromes with increased histamine turnover. It has been found that monoamine oxidase inhibitors block the cytosolic metabolism of 5-HT but not its uptake, while several drugs, including volatile anesthetic agents, block uptake but not intracellular metabolism [74].

Because it is not lipophilic, the pulmonary uptake of 5-HT is an active process, predominately via endothelial cells and with some variability between species. Several details of this uptake have been delineated as an ATPase-dependent active carrier process [75]. The pulmonary uptake of 5-HT by the lung is typically reported to be 90% or greater, meaning that little 5-HT reaches the systemic vasculature under normal circumstances. This model of production and uptake of 5-HT plays a pivotal role in several pathological processes relevant to clinical anesthesiology. In carcinoid syndrome, for example, the right heart receives a high concentration of 5-HT (and other substances) before being extracted and metabolized by the pulmonary circulation. This is thought to be the reason that the right heart shows the greatest myocardial and valvular injury in this syndrome [76–78]. This model is supported by other clinical observations. The valvular injury of substances related to 5-HT such as methysergide and ergotamine, those that increase 5-HT such as the infamous fenfluramine, and more recently the recreational drug "ecstasy" (3,4-methylenedioxymethamphetamine), known to activate 5-HT receptors, are all similar to carcinoid cardiac disease [79, 80]. Additionally, when an intracardiac right-to-left shunt is present in the carcinoid patient with bypass of the pulmonary circulation, the left heart demonstrates valvular injury similar to that of the right heart [81].

Pulmonary embolism presents another clinical situation pertinent to 5-HT activity. It has long been appreciated that the mass effect of embolism does not, in itself, account for the typical cardiopulmonary consequences. The platelet aggregation and activation associated with acute pulmonary embolism results in degranulation with the release of 5-HT, well known to be a potent vasoconstrictor and to increase bronchial smooth muscle tone. This release of 5-HT and, perhaps, decreased local uptake of 5-HT are postulated to cause local and regional vascular changes [82]. Other actions of elevated 5-HT, such as promotion of further platelet aggregation and inhibition of the vasodilating prostacyclin likely also play a role in the full response to pulmonary embolism [83]. The infusion of a serotonin antagonist in animals was found to attenuate the increase in pulmonary pressures of pulmonary embolism [84], supporting the role of 5-HT in this response.

Histamine, in contrast to 5-HT, has almost no uptake in the pulmonary circulation. Lung homogenates are capable of histamine metabolism [85], but the intact lung appears to lack an uptake mechanism for histamine.

Just as the lung has the enzymes to metabolize both histamine and serotonin but the ability to take up only serotonin,

its uptake of catecholamines also demonstrates marked selectivity. Norepinephrine demonstrates a 35–50% first-pass uptake with subsequent metabolism by catechol-O-methyltransferase (COMT), MAO, aldehyde reductase, and aldehyde dehydrogenase [86]. Dopamine and epinephrine, however, have essentially no uptake although they would be susceptible to the cytosolic enzymes, as again proven by cell homogenates. The synthetic catecholamine isoproterenol also has no appreciable uptake by the lung.

Arachidonic Acid Metabolites

Extensive production and metabolism of arachidonic acid derivatives occurs in the lung. The term eicosanoids refers to the 20-carbon carboxylic acids derived from the metabolism of the lipid membrane component icosatetraenoic acid, more commonly known as arachidonic acid. The action of phospholipase A₂ converts the esterified form as found in the membrane and releases arachidonic acid from structural glycerol. Once free, arachidonic acid may follow three main metabolic pathways in the lung. The lipoxygenase pathway produces leukotrienes, lipoxins, and some of the hydroxyeicosatetraenoic acids (HETEs). The cyclo-oxygenase (COX) pathway produces prostaglandins, thromboxane, and prostacyclin. The cytochrome P-450 mono-oxygenase system produces *cis*-epoxyeicosatrienoic acids and HETEs that are different than the products of the lipoxygenase pathway.

The lipoxygenase pathways produce leukotrienes and lipoxins. The formation of all leukotrienes starts from a common point. 5-Lipoxygenase, located in the perinuclear cytosol, responds to increased calcium in concert with its activating protein to generate 5-hydroperoxy-eicosatetraenoic acids (5-HPTE) from arachidonic acid. A dehydrase then yields the relatively unstable leukotriene A₄ (LTA₄), which may undergo transformation by epoxide hydrolase (LTA₄ hydrolase) to LTB₄ which leaves the cell via a transport protein. The alternative pathway for LTA₄ is via LTC₄ synthase to form LTC₄, which is converted by nonspecific interstitial peptidases to the leukotrienes LTD₄ and LTE₄ (commonly referred to as slow reacting substance of anaphylaxis). Whereas closely related prostanoids (see below) demonstrate opposing biological actions, the leukotrienes uniformly promote inflammatory responses in the lung. They are responsible for bronchoconstriction and increased pulmonary vascular permeability, are chemotactic and chemokinetic for neutrophils, and facilitate eosinophil degranulation [87–89]. They are produced by activated inflammatory cells within the lung as well as those arriving in response to inflammation. It should be no surprise that leukotrienes have been the subject of investigation in processes ranging from hypoxic pulmonary vasoconstriction in normal and damaged lungs [90, 91] to the pathogenesis of adult respiratory distress syndrome (ARDS) [92–94] and asthma [95]. This work has been especially fruitful in the case of asthma, for which leukotriene modifiers are a mainstay of treatment [96–98].

There appears to be little specialized pulmonary uptake or metabolism of the leukotrienes beyond the inactivation of LTB₄ and LTC₄ by neutrophils in the lung. Nonspecific hydroxylation and carboxylation of leukotrienes also occur in the interstitium, similar to that of other tissues [99].

The lipoxins have been identified as critical factors in the resolution of inflammation throughout the body, now seen more as an active process than the simple “burn out” of pro-inflammatory processes [100, 101]. There are three main synthetic routes of lipoxin formation, involving interactions of products from 5-lipoxygenase, 15-lipoxygenase, and/or 12-lipoxygenase, with the eventual formation of the two lipoxins, the positional isomers lipoxin A₄ (LxA₄) and B₄ (LxB₄). The lipoxins have a variety of antiinflammatory effects. They inhibit eosinophil and neutrophil chemotaxis and adhesion, as well as natural killer cell activation [102–105]. They are endothelium-dependent vasodilators of both pulmonary and systemic vasculature [106]. The lipoxins have been investigated extensively for their role in lung physiology and disease. Asthma, in particular, has received a great deal of attention [107]. Work thus far indicates that lipoxins are decreased in the sputum [108] and blood [109] of patients with severe asthma. The balance between leukotriene and lipoxin activity, in particular, has been found related to disease severity [110], raising the possibility of inducing lipoxin activity [111] as an adjunct to leukotriene modifiers. The role of lipoxins has also been considered in the active resolution of acute lung injury [112].

The lipoxins are predominately taken up by circulating monocytes with subsequent dehydrogenation [113]. No specific pulmonary uptake or metabolism of lipoxins has been described.

As implied by its name, COX catalyzes the cyclization and oxygenation of arachidonic acid, producing prostaglandin PGG₂, which is converted by nonspecific peroxidase(s) to the unstable precursor PGH₂. There are subtypes of COX, most notably COX-1 and COX-2. There has been great interest in COX-2 since its discovery in the 1990s because its inhibition was hoped to be more specific in controlling pain and inflammation without injury to the gastroduodenal mucosa [114, 115]. Although effective, the emergence of a small but real increase in cardiovascular risk of COX-2 inhibitors [116] has tempered their use. Complicating this issue further is that many of the “traditional” COX inhibitors such as acetaminophen, salicylates, and the nonsteroidal antiinflammatory agents ibuprofen and naproxen show only slightly less COX-2 avidity than some of the newer COX-2 inhibitors.

Following the production of PGH₂, the metabolic pathway divides into branches producing the various bioactive prostanoids; the enzymes of particular interest here are PGD synthase, PGE synthase, prostacyclin synthase, and thromboxane synthase. The final products of these pathways typically have opposed or balancing effects locally and regionally. Prostaglandin E₂ (PGE₂) and PGI₂ are bronchodilators, for example, while PGF_{2α}, PGD₂, and thromboxane A₂ (TXA₂) cause bronchoconstriction. Similarly, PGD₂, PGE₂, PGF_{2α},

and TXA₂ are potent vasoconstrictors, while PGE₁ and PGF₂ are vasodilators.

Pulmonary endothelial cell cultures demonstrate virtually all COX pathway products to some extent, but the level of *in vivo* production is less clear. PGI₂ appears to be continuously produced, with modulation by vascular flow [117]. PGD₂, PGE₁, PGE₂, PGI₂, PGF_{2 α} , and TXB₂ have all been found to be produced by human lungs, although under varying circumstances [118, 119].

The discussion of the pulmonary metabolism of COX products includes the now familiar theme of a broad range of intracellular enzymes (by cell culture and cellular homogenate investigation) but selective uptake. In this way, at least 80–90% of PGD₁, PGE₂, and PGF_{2 α} are taken up and metabolized in a first-pass through intact pulmonary circulation; but, PGA₁, PGA₂, and PGI₂ demonstrate essentially no uptake [23, 120, 121]. TXA₂, a relatively unstable compound, presents a special case in the discussion of pulmonary uptake. TXA₂ undergoes hydrolysis in the blood, forming TXB₂. It is TXB₂ that is taken up by a carrier for cytosolic metabolism and that is often utilized as an investigative marker of TXA₂ activity [122].

The P-450 mono-oxygenase system provides three pathways of arachidonic acid metabolism which result in epoxyeicosatetraenoic acids (EETs), HETEs, or di-hydroxyeicosatetraenoic acids (dHETEs). These pathways are not unique to the endothelium, epithelium, and smooth muscle of the lung, being found in several other organs, including the gastrointestinal tract, liver, and kidney [123]. Subfamilies of cytochrome P-450 systems have been identified within the lung. The CYPA4 family produces 20-HETE, while the CYP2J family is found in epithelial, bronchial, and vascular smooth muscle cells, as well as endothelial and alveolar macrophages [124].

The HETEs and EETs have been shown experimentally to affect pulmonary vascular and bronchomotor tone. 20 HETE and 5, 6, 11, and 12-EETs all have relaxing effects on both the lung vasculature and airways [125, 126]. They are further known to have general antiinflammatory effects, to modulate reperfusion injury, and to inhibit platelet aggregation. Within the lung, 15-HETE and 20-HETE may both modify hypoxic vasoconstriction [127].

Natriuretic Peptides

The natriuretic peptides currently consist of, in order of their discovery during the 1980s, atrial natriuretic peptide (ANP), brain natriuretic peptide, and C-type natriuretic peptide. ANP has received the most attention in terms of pulmonary pharmacokinetics. It is a pulmonary artery (and to a lesser extent, venous) vasodilator whose action is independent of endothelial function. ANP is known to interact with the renin–angiotensin–aldosterone system at several points. Best described are suppression of renin release, decrease of angiotensin converting enzyme activity, and blocking of aldosterone release. These actions promote natriuresis and diuresis.

ANP is mainly produced in the cardiac atria, but both ANP and its prohormone have been found in the human fetal lung [128] and adult pulmonary veins [129]. Lung production is apparently suppressed by hypovolemia and increased with hypoxemia, hypervolemia, and in the presence of glucocorticoids. In terms of elimination, the rabbit lung demonstrates a 25% first-pass uptake of ANP [130].

Other Endogenous Substances

The number of substances handled by the lung and the intricacies of their metabolism precludes full discussion here. For the interested reader, several historically and/or clinically important substances are listed in Table 7.3 and references are provided for the activation of cortisone to cortisol in health [131, 132] and disease [133], the behavior of endothelin in several clinical circumstances [70, 134, 135], and new perspectives on purine metabolism by endothelial ecto-enzymes [133].

The Lung as Vascular Reservoir and Filter

The volume of blood within the lungs under various conditions has been a subject of investigation for over 80 years [136]. What has come to be known is that the pulmonary vasculature in health has remarkable capacitance, allowing it to accept the wide ranges of right ventricular output with minimal change in pressure. This ability to load and offload volume allows the lungs to serve as a vascular reservoir to meet the preload needs of the left heart as they change due to factors such as posture, exercise, and daily volume shifts [137]. The role of pulmonary vascular capacitance is also emerging in our understanding of disease processes relevant to clinical anesthesiology. Models of heart failure, for example, now incorporate the role of vascular compliance in general and the pulmonary vasculature capacitance and permeability specifically [138]. Also of interest to anesthesiologists, researchers have found that following the release of tourniquet in total knee arthroplasty, there is an actual decrease in pulmonary vascular resistance. A clue to the mechanism of this finding was metabolic evidence of increased endothelial recruitment with this obligatory microembolism [139].

The unique anatomical position of the lungs as they receive the entire right heart output allows them to serve as physical filters, in much the same way that they metabolically play a pivotal role in the uptake of endogenous substances and xenobiotics. The literature commonly alludes to the ability of 350 and even 500 μ m glass beads to pass through the pulmonary vasculature in animal models. Given that normal pulmonary capillaries have a diameter of 7–10 μ m, this implies other arterio-venous communications under normal conditions. Recent work in isolated, but normally ventilated, animal and human lungs and, especially, exercised human subjects imply a more complicated picture. It now appears that, indeed, arterio-venous passage of

TABLE 7.3. Lung effects on endogenous substances relevant to the anesthesiologist.

Group	Impact of passage through the pulmonary circulation		
	Activated	Minimal or none	First-pass uptake and/or metabolism
<i>Peptides</i>	Angiotensin I	Angiotensin II Vasopressin Oxytocin Atrial natriuretic peptide	Endothelins Bradykinin
<i>Steroids</i>	Cortisone		Beclomethasone Progesterone
<i>Purine family</i>			Adenosine Adenosine phosphates (AMP, ADP, ATP)
<i>Arachidonic acid family</i>		PGA ₂ Prostacyclin (PGI ₂)	PGD ₂ PGE ₂ PGF ₂ Leukotrienes
<i>Biogenic amines</i>		Dopamine Epinephrine Histamine	5-HT Norepinephrine

particles larger than 50 μm occur in isolated lungs, although more than 99% of such glass microspheres are trapped by the lungs [140]. In human volunteers, aggregated albumin tagged with technetium-99 and with diameters of 7–25 μm was found to have about 0.7% transpulmonary passage at rest. This rose to 3% passage with exercise, as demonstrated by aggregate trapping in systemic capillaries. This implies the recruitment of intrapulmonary arterio-venous pathways with exercise which presumably allow decreased resistance to flow but compromise the lung's competence as a mechanical filter [141]. The lung's protection of systemic circulation from embolus can also, of course, be completely subverted by anatomic variants and pathological states. The latter is exemplified by the hepatopulmonary syndrome's intrapulmonary vascular dilatations, which have been associated with patient injury from embolism [142]. The patent foramen ovale and its potential for catastrophic embolic phenomena in the perioperative period [81, 141, 143] have long been appreciated and feared by anesthesiologists as the classic anatomic variant which bypasses the protective filtration of the pulmonary vasculature.

The Respiratory Epithelium

The lung defends the body not only by mechanical filtration and metabolism of substances from the blood, but also from agents that are air-borne. The respiratory epithelium represents a huge surface area that is a gateway from the outside world to the exquisitely delicate alveoli; a path taken by both life sustaining oxygen and potentially damaging particles and gasses. This defensive challenge is especially impressive when considering both the wide range of conditions to which the modern human is exposed and the simple fact that even a somewhat sedentary adult can be expected to inhale well over 10,000 L of gas from his/her environment in a day. The discussion below will briefly review the structure and function of

this system and then the way in which it provides protection through the mucociliary apparatus, trapping of particles, and response to particles and pathogens.

The Cells of the Respiratory Epithelium

While some 50 distinct cell types have been identified in the human airway [144], our discussion will focus on those most important to the lung's nonrespiratory functions.

Ciliated Columnar Cells

These cells are the most common of the respiratory epithelium. Their most obvious defining feature is several hundred cilia moving at a rate of about 12 cycles per second, always toward the trachea. As might be expected, this process requires large energy expenditures, and, in fact, the cells have extensive populations of mitochondria. The cellular architecture and shape change according to position in the respiratory tract. In the nose, pharynx, and large airways, the columnar cells are pseudostratified, layered over the basal cells which are thought to be the stem cells for both ciliated and goblet cells. Moving down the bronchi, they gradually thin to a single layer. Further still, in the bronchioles, the columnar cells transition to a layer of cuboidal cells and then, approaching the terminal airways, they mix with type I alveolar cells.

Goblet Cells

These specialized columnar epithelial cells can rapidly secrete mucins (high molecular weight mucous glycoproteins) which provide a protective layer over the epithelium when it combines with other lipid, glycoconjugate, and protein components [145]. Mucin is released by exocytosis in response to a variety of stimuli such as dust, microorganisms, fumes, and debris within the airway. Hyperplasia in response to chronic stimulation is

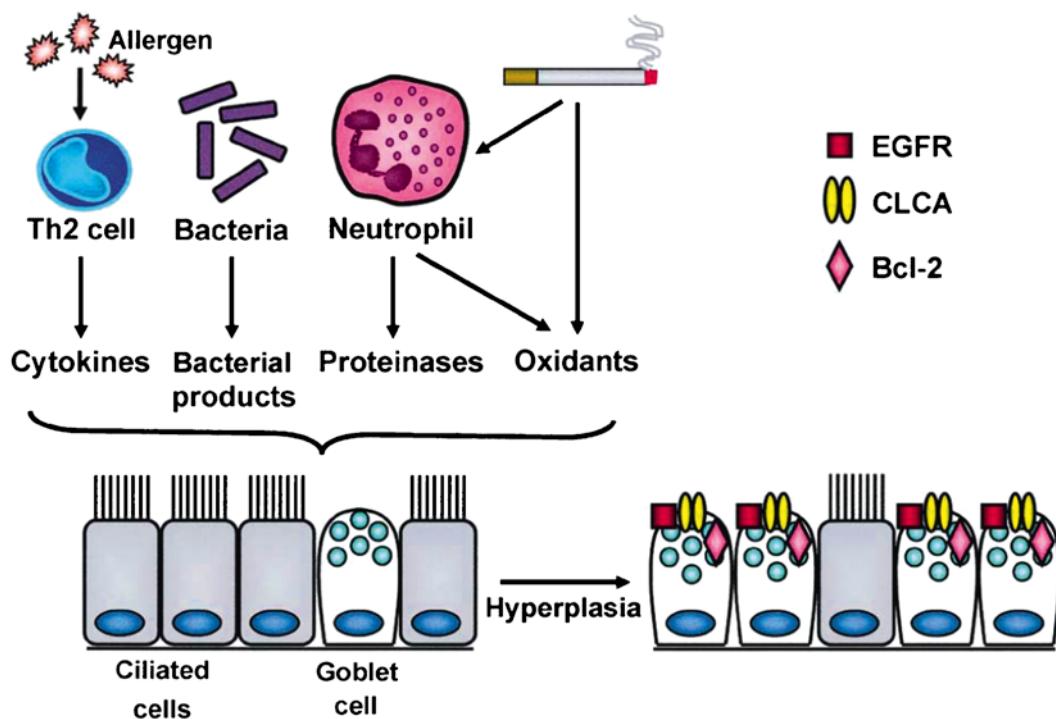


FIG. 7.3. Airway goblet cell hyperplasia. Simplified schematic outlining selected pathways generating increased epithelial mucin production. Cytokines (e.g., interleukin-4, -9 and -13), bacterial products (e.g., lipopolysaccharide and lipoteichoic acid), proteinases (e.g., elastase and cathepsin G), and oxidants from T helper-2 (Th2) lymphocytes, bacteria, neutrophils, and cigarette smoke upregulate mucin production and/or induce goblet cell hyperplasia with associated increases in expression of epidermal growth factor receptors (EGFR), calcium activated chloride channels (CLCA), and the antiapoptotic factor Bcl-2. Note: not all stimuli have yet been shown to induce expression of each of EGFR, CLCA and Bcl-2. In addition, production of new goblet cells appears to involve differentiation of nongranulated epithelial cells rather than goblet cell division (reproduced with permission. Rogers [45]. Copyright Elsevier).

a hallmark of the goblet cell population (Fig. 7.3) and typical of disease processes such as asthma, bronchitis, and cystic fibrosis [146].

Submucosal Secretory Cells

There are actually two types of submucosal secretory cells. Both are associated with the submucosal glands of the trachea and large bronchi. These glands are innervated by cholinergic fibers from the vagus [147] and are located in the submucosa between the smooth muscle and cartilage plate. The serous type cells account for more than half of the submucosal gland in health and contain multiple secretory granules. Proteoglycans, lysozyme, lactoferrin, IgA receptor complex, peroxidase, and antiproteases are amongst the contents of these granules. The mucous type cells are columnar cells with a high density of cell granules containing mucin. It is thought that serous cells transdifferentiate to mucous cells in response to injury from inhaled agents and the resulting predominance of mucous cells plays a role in the change of the character of mucus in response to injury. While it is accepted that both the submucosal secretory cells and goblet cells contribute

to airway mucus, there is apparent variability in the relative contribution of these cells on the basis of airway level, experimental model, and species [148–151].

Clara Cells

Clara cells (nonciliated bronchial secretory cells) are normally found predominately in the terminal bronchioles (Fig. 7.4). Their granules secrete Clara cell secretory protein (CCSP), the function of which is poorly defined. In an animal model, antigenic challenge results in proliferation of tracheobronchial Clara cells that secret not only CCSP, but also demonstrate secretion of mucin [151]. Conversely, in normal humans, bronchiolar goblet cells have been found to secrete CCSP, leading to speculation that Clara cells may be goblet cell precursors [152], as well as progenitors of the epithelium [153].

Mast Cells

Mast cells are located throughout the lung, from typical locations under the airway epithelium and in the alveolar septum to those freely positioned in the airway. They have traditionally

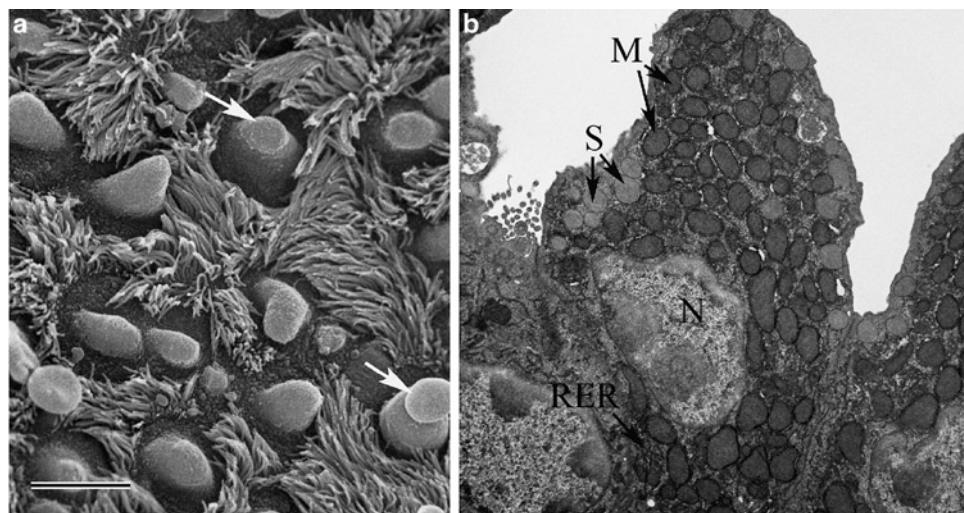


FIG. 7.4. (a) Scanning electron micrograph of the lining of the proximal bronchiole of a rat showing Clara cells, some of which are undergoing apocrine secretion (arrows), surrounded by ciliated cells (bar=10 μ m). (b) Transmission electron micrograph of a terminal bronchiolar Clara cell. Numerous mitochondria (M), secretory granules (S), rough endoplasmic reticulum (RER), and the basal nucleus (N) are indicated (reproduced with permission. Reynolds and Malkinson [53]. Copyright Elsevier).

been associated with acquired immunity, but recent evidence indicates that mast cells also have important roles in innate immunity and inflammatory regulation [154]. Specifically, their role as sentinel for innate immunity seems to bridge the classic with the more recently appreciated roles [155].

Macrophages and Monocytes

Macrophages and monocytes can be categorized as (1) airway and alveolar macrophages, (2) interstitial macrophages, and (3) pulmonary vascular monocytes. This scheme does not include the monocyte derivative dendritic cells. There are limited data regarding the sparse interstitial macrophage population, mostly from animal preparations. There is no evidence that the intravascular monocytes of the lung are particularly different than monocytes throughout the body's vascular system, transforming into macrophages within the tissue to which they migrate.

The alveolar macrophages must routinely phagocytize a dizzying array of invaders of the airspace. These include dust and particulates as well as bacteria, yeasts, and other organic and inorganic debris. Phagosomes initially envelope the ingested target and then are merged with lysosomes. The latter contain hydrolytic enzymes, which efficiently destroy the majority of bacteria, yeasts, and debris encountered. For some microorganisms (e.g., mycobacteria or many gram-negative bacteria) and materials, the lysosomal system is not effective. In this case, secondary lysosomes are now used essentially as storage areas, where the material is isolated for the life of the macrophage. The fate of these laden cells is not uniform. It appears that some are swept away by the mucociliary apparatus for mechanical elimination and others remain in the lung for as

long as months before dying and releasing their sequestered contents for uptake by successor macrophages. There has been recent attention to the translocation of particles from the lung to lymph nodes and other organs [156, 157], presumably in conjunction with alveolar macrophage activity.

Alveolar Epithelial Cells

Alveolar epithelial type I and type II cells (also referred to as type I and II pneumocytes) line the terminal alveoli. Type I cells are thin sheets lining the alveoli with each covering several capillaries. The tight junctions between cells are well described and thought to provide only a 1- μ m gap under normal circumstances. Historically thought to serve as a barrier to the movement of solutes and water into the alveoli, more recent work with sodium and chloride transporters has found evidence of active epithelial mechanisms for fluid transport in both health and diseased states [158, 159]. Type II alveolar epithelial cells tend to be clustered at alveolar juncture points. They are cuboidal cells with lamellar bodies in the cytoplasm and numerous mitochondria. The lamellar bodies are inclusions of variable size and composed of stacked layers of membrane-like material. It is this material which is processed and released as surfactant by the type II cell [160]. Four types of surfactant proteins A, B, C, and D (SP-A through SP-D), have been identified. SP-A and SP-D modulate surfactant release, while SP-B and SP-C stabilize the surfactant monolayer discussed below [161]. SP-B is the protein absolutely required for survival, but important contributions have been discovered from the other SP proteins. SP-A and SP-D, for example, play immune roles by direct antimicrobial activity and enhancement of macrophage recognition of microorganisms.

Functions of the Respiratory Epithelium

The functions of the respiratory epithelium that will be reviewed here include maintenance of the complex liquid film of the airway, humidification, removal of inhaled materials, and response to inhaled pathogens.

Airway Surface Film

The surface liquid of the airway, in health, is about 10 μm thick. It consists of two layers, namely, the periciliary sol underneath a second layer of mucus gel. The sol is a low-viscosity watery liquid that surrounds the cilia. The mucus, as discussed previously, is produced by the submucosal glands and goblet cells in response to a variety of irritants. The cilia are too tightly arranged for the mucus gel to find its way between cilia, thus the gel layer contacts only the ciliary tips along its bottom edge. The cilia, then, are free to move in their well-characterized rhythmic pattern with relatively less resistance from the minimally viscous sol. In this manner, the cilia propel the mucous layer toward the trachea at a rate of 3–4 mm min^{-1} [162]. The thickness of the layers of this system, especially the sol, must be maintained within very narrow tolerances for mechanical efficiency. This is achieved in large extent by simple osmotic gradient and probably accounts for much of the adjustment that occurs as larger amounts of mucus converge in the larger airways. Adjustments of sol osmolarity to effect this mechanism occur through the activity of the amiloride-sensitive chloride channel, more commonly referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Indeed, the ravages of cystic fibrosis are now thought to start at least in part because of the relative depletion of the sol, emphasizing the delicate nature of the system just described [163]. The antimicrobial capabilities of the mucociliary apparatus will be discussed below.

Humidification

The respiratory system has enormous capacity to humidify inspired gas. At rest, air is completely saturated with water vapor as it passes through the nose and upper airway, before it reaches the trachea. As minute ventilation (MV) increases, smaller and smaller airways are required to contribute to humidification, such that at a MV of 50 L min^{-1} , airways of only a few millimeters diameter receive incompletely humidified gas [164]. The airways do reclaim some of the heat and moisture imparted on the inhaled gas during its exhalation. Thus, bypassing of the nasopharyngeal passages and upper trachea by devices such as endotracheal tubes not only decreases humidification of the gasses delivered to the distal airways, but also cheats the opportunity to recoup heat and moisture on exhalation.

Removal of Inhaled Particles

The regions of the respiratory tract in which particles are deposited depend upon respiratory pattern, environmental conditions, and the nature of the particles themselves. Accepting these variations, it is possible to generalize particle behavior under normal circumstances. Particles larger than 10 μm (e.g., dust and particulates from low-grade petroleum combustion) are often trapped at the level of the nose or pharynx. Those that enter the airway of the lung, and particles of 3–10 μm , are caught on the liquid film layer and transported out of the lung for swallowing or expectoration as previously described. They tend to be deposited in higher concentration in areas of high turbulence such as airway bifurcations. Particles smaller than 3 μm may reach the alveoli. They will either be subsequently exhaled or settle in the alveolus, where they will be subject to the activity of macrophages as discussed in a previous section. There are, of course, particular substances that instigate a detrimental response from the body, for example asbestos with resultant pulmonary fibrosis.

Response to Inhaled Organisms

There are several mechanisms with which the airway defends the body against inhaled microorganisms. The first is simple impact and capture by the nasal and pharyngeal mucosa with subsequent swallowing and destruction in the hostile gastrointestinal tract or expectoration. Those organisms that enter the lung may be similarly trapped on the surface film and moved out of the lung by ciliary action. The surface film is more than a simple transport mechanism, having a variety of antimicrobial mechanisms. These capabilities make teleological sense, because the potentially damaging agents are not immediately removed.

Surfactants are best known for their ability to reduce surface tension and thus equalize pressures within airspaces of differing size. Less appreciated is the fact that SP-A and SP-D (following terminology introduced in the discussion of type II alveolar cells) are members of the collectin protein family. Collectins have an N-terminal collagen type region and a C-terminal lectin region that bind carbohydrates. The C-terminal's preferential binding site is nonhost oligosaccharides, giving them the ability to opsonize bacterial and viral pathogens and to facilitate macrophage phagocytosis [165]. SP-A and SP-D are also known to be directly antimicrobial, without immune cells, against a variety of pathogens [166, 167].

The surface films of the large bronchi (and the mucosa of the nasopharynx) have generous amounts of IgA, which acts as an opsonin and has a role in complement induction. In smaller airways and alveoli, IgG becomes the predominant surface antibody in normal circumstances.

Active defensive responses of the airway include the release of lactoferrin by neutrophils and epithelial cells, as well as lysozymes and defensins from neutrophils. Stimulated

bronchial epithelial cells can also secrete and/or facilitate adhesion molecules, cytokines and chemokines, and eventually, growth factors and collagen.

Summary

Historically, practitioners of the medical arts from around the globe viewed the lung as a defender of the body from a hostile outside world, and as a trusted modulator of its internal processes. More recently, respiratory function became the focus of attention with advances that have been central to the development of anesthesiology and upon which modern clinicians base much of our practice in cardiopulmonary medicine. The purpose of this discussion, which returns to the concepts of lung as protector and minister, has been to highlight important nonrespiratory lung functions in terms of both current areas of discovery and clinical implications. It is hoped that the reader will agree that familiarity with these aspects of pulmonary function are pivotal to a complete understanding of the lung and to the advancement of clinical practice.

References

1. Major R. *A history of medicine*. Springfield: Thomas; 1954.
2. Lumb AB. The history of respiratory physiology. In: Lumb AB, editor. *Nunn's applied respiratory physiology*. 6th ed. Oxford: Butterworth-Heinemann; 2005.
3. Shoja MM, Tubbs RS. The history of anatomy in Persia. *J Anat*. 2007;210(4):359–78.
4. Simionescu M. Lung endothelium: structure-function correlates. In: Crystal RG, editor. *Lung: scientific foundations*. New York: Raven Press; 1991. p. 301–21.
5. Klein IK, Predescu DN, Sharma T, Knezevic I, Malik AB, Predescu S. Intersectin-2L regulates caveola endocytosis secondary to Cdc42-mediated actin polymerization. *J Biol Chem*. 2009;284(38):25953–61.
6. Parat M, Kwang WJ. The biology of caveolae: achievements and perspectives. *International review of cell and molecular biology*. Vol. 273. Academic; 2009. p. 117–62.
7. Ryan US, Ryan JW. Relevance of endothelial surface structure to the activity of vasoactive substances. *Chest*. 1985;88 (4 Suppl):203S–7.
8. Ryan JW, Smith U. Metabolism of adenosine 5'-monophosphate during circulation through the lungs. *Trans Assoc Am Physicians*. 1971;84:297–306.
9. Vane JR. The release and fate of vaso-active hormones in the circulation. *Br J Pharmacol*. 1969;35(2):209–42.
10. Dawidowicz ALP, Fornal EPD, Mardarowicz MPD, Fijalkowska APD. The role of human lungs in the biotransformation of propofol. *Anesthesiology*. 2000;93(4):992–7.
11. Hiraoka H, Yamamoto K, Miyoshi S, et al. Kidneys contribute to the extrahepatic clearance of propofol in humans, but not lungs and brain. *Br J Clin Pharmacol*. 2005;60(2):176–82.
12. de Graaf IAM, Koster HJ. Cryopreservation of precision-cut tissue slices for application in drug metabolism research. *Toxicology In Vitro*. 2003;17(1):1–17.
13. Klem C, Dasta JF, Reiley TE, Flancbaum LJ. Pulmonary extraction of dobutamine in critically ill surgical patients. *Anesth Analg*. 1995;81(2):287–91.
14. Hayashi Y, Sumikawa K, Yamatodani A, Kamibayashi T, Mamamoto T, Kuro M. Quantitative analysis of pulmonary clearance of exogenous dopamine after cardiopulmonary bypass in humans. *Anesth Analg*. 1993;76(1):107–12.
15. Matot I, Pizov R. Pulmonary extraction and accumulation of lipid formulations of amphotericin B. *Crit Care Med*. 2000;28(7): 2528–32.
16. Upton RN, Doolee DJ. Kinetic aspects of drug disposition in the lungs. *Clin Exp Pharmacol Physiol*. 1999;26(5–6):381–91.
17. Serabjit-Singh CJ, Nishio SJ, Philpot RM, Plopper CG. The distribution of cytochrome P-450 monooxygenase in cells of the rabbit lung: an ultrastructural immunocytochemical characterization. *Mol Pharmacol*. 1988;33(3):279–89.
18. Pacifici GM, Franchi M, Bencini C, Repetti F, Di Lascio N, Muraro GB. Tissue distribution of drug-metabolizing enzymes in humans. *Xenobiotica*. 1988;18(7):849–56.
19. Litterst CL, Minnaugh EG, Reagan RL, Gram TE. Comparison of in vitro drug metabolism by lung, liver, and kidney of several common laboratory species. *Drug Metab Dispos*. 1975;3(4): 259–65.
20. Taeger K, Weninger E, Schmelzer F, Adt M, Franke N, Peter K. Pulmonary kinetics of fentanyl and alfentanil in surgical patients. *Br J Anaesth*. 1988;61(4):425–34.
21. Waters CM, Krejcie TC, Avram MJ. Facilitated uptake of fentanyl, but not alfentanil, by human pulmonary endothelial cells. *Anesthesiology*. 2000;93(3):825–31.
22. Boer F, Bovill JG, Burn AG, Mooren RA. Uptake of sufentanil, alfentanil and morphine in the lungs of patients about to undergo coronary artery surgery. *Br J Anaesth*. 1992;68(4):370–5.
23. Boer F, Olofson E, Bovill JG, et al. Pulmonary uptake of sufentanil during and after constant rate infusion. *Br J Anaesth*. 1996;76(2):203–8.
24. Davis ME, Mehendale HM. Absence of metabolism of morphine during accumulation by isolated perfused rabbit lung. *Drug Metab Dispos*. 1979;7(6):425–8.
25. Roerig DL, Kotly KJ, Vucins EJ, Ahlf SB, Dawson CA, Kampine JP. First pass uptake of fentanyl, meperidine, and morphine in the human lung. *Anesthesiology*. 1987;67(4):466–72.
26. Persson MP, Wiklund L, Hartvig P, Paalzow L. Potential pulmonary uptake and clearance of morphine in postoperative patients. *Eur J Clin Pharmacol*. 1986;30(5):567–74.
27. Beaufort TM, Proost JH, Houwertjes MC, Roggeveld J, Wierda JM. The pulmonary first-pass uptake of five nondepolarizing muscle relaxants in the pig. *Anesthesiology*. 1999;90(2):477–83.
28. Bertler A, Lewis DH, Lofstrom JB, Post C. In vivo lung uptake of lidocaine in pigs. *Acta Anaesthesiol Scand*. 1978;22(5):530–6.
29. Post C, Eriksdotter-Behm K. Dependence of lung uptake of lidocaine in vivo on blood pH. *Acta Pharmacol Toxicol (Copenh)*. 1982;51(2):136–40.
30. Krejcie TC, Avram MJ, Gentry WB, Niemann CU, Janowski MP, Henthorn TK. A recirculatory model of the pulmonary uptake and pharmacokinetics of lidocaine based on analysis of arterial and mixed venous data from dogs. *J Pharmacokinet Biopharm*. 1997;25(2):169–90.
31. Hasegawa K, Yukioka H, Hayashi M, Tatekawa S, Fujimori M. Lung uptake of lidocaine during hyperoxia and hypoxia in the dog. *Acta Anaesthesiol Scand*. 1996;40(4):489–95.

32. Sjostrand U, Widman B. Distribution of bupivacaine in the rabbit under normal and acidotic conditions. *Acta Anaesthesiol Scand Suppl.* 1973;50:1–24.
33. Irestedt L, Andreen M, Belfrage P, Fagerstrom T. The elimination of bupivacaine (Marcain) after short intravenous infusion in the dog: with special reference to the role played by the liver and lungs. *Acta Anaesthesiol Scand.* 1978;22(4):413–22.
34. Rothstein P, Cole JS, Pitt BR. Pulmonary extraction of [³H] bupivacaine: modification by dose, propranolol and interaction with [¹⁴C]5-hydroxytryptamine. *J Pharmacol Exp Ther.* 1987;240(2):410–4.
35. Kietzmann D, Foth H, Geng WP, Rathgeber J, GundertRemy U, Kettler D. Transpulmonary disposition of prilocaine, mepivacaine, and bupivacaine in humans in the course of epidural anaesthesia. *Acta Anaesthesiol Scand.* 1995;39(7):885–90.
36. Sharrock NE, Mather LE, Go G, Sculco TP. Arterial and pulmonary arterial concentrations of the enantiomers of bupivacaine after epidural injection in elderly patients. *Anesth Analg.* 1998;86(4):812–7.
37. Palazzo MG, Kalso EA, Argiras E, Madgwick R, Sear JW. First pass lung uptake of bupivacaine: effect of acidosis in an intact rabbit lung model. *Br J Anaesth.* 1991;67(6):759–63.
38. Chang DH, Ladd LA, Wilson KA, Gelgor L, Mather LE. Tolerance of large-dose intravenous levobupivacaine in sheep. *Anesth Analg.* 2000;91(3):671–9.
39. Ohmura S, Kawada M, Ohta T, Yamamoto K, Kobayashi T. Systemic toxicity and resuscitation in bupivacaine-, levobupivacaine-, or ropivacaine-infused rats. [see comment]. *Anesth Analg.* 2001;93(3):743–8.
40. Ohmura S, Sugano A, Kawada M, Yamamoto K. Pulmonary uptake of ropivacaine and levobupivacaine in rabbits. *Anesth Analg.* 2003;97(3):893–7.
41. Mather LE, Copeland SE, Ladd LA. Acute toxicity of local anesthetics: underlying pharmacokinetic and pharmacodynamic concepts [see comment]. *Reg Anesth Pain Med.* 2005;30(6):553–66.
42. Heavner JE. Let's abandon blanket maximum recommended doses of local anesthetics [comment]. *Reg Anesth Pain Med.* 2004;29(6):524.
43. Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept [see comment]. *Reg Anesth Pain Med.* 2004;29(6):564–75; discussion 524.
44. Reynolds F. Maximum recommended doses of local anesthetics: a constant cause of confusion [comment]. *Reg Anesth Pain Med.* 2005;30(3):314–6.
45. Groban L. Central nervous system and cardiac effects from long-acting amide local anesthetic toxicity in the intact animal model. *Reg Anesth Pain Med.* 2003;28(1):3–11.
46. Mulroy MF. Systemic toxicity and cardiotoxicity from local anesthetics: incidence and preventive measures. *Reg Anesth Pain Med.* 2002;27(6):556–61.
47. Rosenblatt MA, Abel M, Fischer GW, Itzkovich CJ, Eisenkraft JB. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest [see comment]. *Anesthesiology.* 2006;105(1):217–8.
48. Felice K, Schumann H. Intravenous lipid emulsion for local anesthetic toxicity: a review of the literature. *J Med Toxicol.* 2008;4(3):184–91.
49. Marwick PC, Levin AI, Coetzee AR. Recurrence of cardiotoxicity after lipid rescue from bupivacaine-induced cardiac arrest [see comment]. *Anesth Analg.* 2009;108(4):1344–6.
50. Roerig DL, Kotryl KJ, Dawson CA, Ahlf SB, Gaultier JF, Kampine JP. First-pass uptake of verapamil, diazepam, and thiopental in the human lung. *Anesth Analg.* 1989;69(4):461–6.
51. Pedraz JL, Lanao JM, Hernandez JM, Dominguez-Gil A. The biotransformation kinetics of ketamine "in vitro" in rabbit liver and lung microsome fractions. *Eur J Drug Metab Pharmacokinet.* 1986;11(1):9–16.
52. Henthorn TK, Krejcie TC, Niemann CU, Enders-Klein C, Shanks CA, Avram MJ. Ketamine distribution described by a recirculatory pharmacokinetic model is not stereoselective. *Anesthesiology.* 1999;91(6):1733–43.
53. Mather LE, Selby DG, Runciman WB, McLean CF. Propofol: assay and regional mass balance in the sheep. *Xenobiotica.* 1989;19(11):1337–47.
54. Kuipers JA, Boer F, Olieman W, Burm AG, Bovill JG. First-pass lung uptake and pulmonary clearance of propofol: assessment with a recirculatory indocyanine green pharmacokinetic model. *Anesthesiology.* 1999;91(6):1780–7.
55. Matot I, Neely CF, Katz RY, Neufeld GR. Pulmonary uptake of propofol in cats. Effect of fentanyl and halothane. *Anesthesiology.* 1993;78(6):1157–65.
56. Le Guellec C, Lacarelle B, Villard PH, Point H, Catalin J, Durand A. Glucuronidation of propofol in microsomal fractions from various tissues and species including humans: effect of different drugs. *Anesth Analg.* 1995;81(4):855–61.
57. Bulger EM, Maier RV. Lipid mediators in the pathophysiology of critical illness. *Crit Care Med.* 2000;28(4 Suppl):N27–36.
58. Upton RN, Ludbrook G. A physiologically based, recirculatory model of the kinetics and dynamics of propofol in man. *Anesthesiology.* 2005;103(2):344–52.
59. Kazama T, Ikeda K, Morita K, Ikeda T, Kikura M, Sato S. Relation between initial blood distribution volume and propofol induction dose requirement [see comment]. *Anesthesiology.* 2001;94(2):205–10.
60. Kazama T, Morita K, Ikeda T, Kurita T, Sato S. Comparison of predicted induction dose with predetermined physiologic characteristics of patients and with pharmacokinetic models incorporating those characteristics as covariates. *Anesthesiology.* 2003;98(2):299–305.
61. Krejcie TC, Jacquez JA, Avram MJ, Niemann CU, Shanks CA, Henthorn TK. Use of parallel Erlang density functions to analyze first-pass pulmonary uptake of multiple indicators in dogs. *J Pharmacokinet Biopharm.* 1996;24(6):569–88.
62. Ryan JW. Processing of endogenous polypeptides by the lungs. *Annu Rev Physiol.* 1982;44:241–55.
63. Orfanos SE, Langleben D, Khouri J, et al. Pulmonary capillary endothelium-bound angiotensin-converting enzyme activity in humans. *Circulation.* 1999;99(12):1593–9.
64. Skidgel RA. Bradykinin-degrading enzymes: structure, function, distribution, and potential roles in cardiovascular pharmacology. *J Cardiovasc Pharmacol.* 1992;20 Suppl 9:S4–9.
65. Chand N, Altura BM. Acetylcholine and bradykinin relax intrapulmonary arteries by acting on endothelial cells: role in lung vascular diseases. *Science.* 1981;213(4514):1376–9.
66. Skidgel RA, Erdos EG. Angiotensin converting enzyme (ACE) and neprilysin hydrolyze neuropeptides: a brief history, the beginning and follow-ups to early studies. *Peptides.* 2004;25(3):521–5.

67. Simke J, Graeme ML, Sigg EB. Bradykinin induced bronchoconstriction in guinea pigs and its modification by various agents. *Arch Int Pharmacodyn Ther.* 1967;165(2):291–301.
68. Collier HO. Humoral factors in bronchoconstriction. *Sci Basis Med Annu Rev.* 1968;308–35.
69. Suguikawa TR, Garcia CA, Martinez EZ, Vianna EO. Cough and dyspnea during bronchoconstriction: comparison of different stimuli. *Cough.* 2009;5:6.
70. Enseleit F, Hurlmann D, Luscher TF. Vascular protective effects of angiotensin converting enzyme inhibitors and their relation to clinical events. *J Cardiovasc Pharmacol.* 2001;37 Suppl 1:S21–30.
71. Muntner P, Krousel-Wood M, Hyre AD, et al. Antihypertensive prescriptions for newly treated patients before and after the main antihypertensive and lipid-lowering treatment to prevent heart attack trial results and seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure guidelines [see comment]. *Hypertension.* 2009;53(4):617–23.
72. Alabaster VA, Bakhle YS. Removal of 5-hydroxytryptamine in the pulmonary circulation of rat isolated lungs. *Br J Pharmacol.* 1970;40(3):468–82.
73. Gommori K, Rao KS, Mehendale HM. Pulmonary synthesis of 5-hydroxytryptamine in isolated perfused rabbit and rat lung preparations. *Exp Lung Res.* 1986;11(4):295–305.
74. Cook DR, Brandom BW. Enflurane, halothane, and isoflurane inhibit removal of 5-hydroxytryptamine from the pulmonary circulation. *Anesth Analg.* 1982;61(8):671–5.
75. Junod AF. Uptake, metabolism and efflux of 14 C-5-hydroxytryptamine in isolated perfused rat lungs. *J Pharmacol Exp Ther.* 1972;183(2):341–55.
76. Righi L, Volante M, Rapa I, Scagliotti GV, Papotti M. Neuroendocrine tumours of the lung. A review of relevant pathological and molecular data. *Virchows Arch.* 2007;451 Suppl 1:S51–9.
77. Shah PM, Raney AA. Tricuspid valve disease. *Curr Probl Cardiol.* 2008;33(2):47–84.
78. Sandmann H, Pakkal M, Steeds R. Cardiovascular magnetic resonance imaging in the assessment of carcinoid heart disease. *Clin Radiol.* 2009;64(8):761–6.
79. Bernheim AM, Connolly HM, Pellikka PA. Carcinoid heart disease. *Curr Treat Options Cardiovasc Med.* 2007;9(6):482–9.
80. Droogmans S, Cosyns B, D'Haenen H, et al. Possible association between 3, 4-methylenedioxymethamphetamine abuse and valvular heart disease. *Am J Cardiol.* 2007;100(9):1442–5.
81. Mizuguchi KA, Fox AA, Burch TM, Cohn LH, Fox JA. Tricuspid and mitral valve carcinoid disease in the setting of a patent foramen ovale. *Anesth Analg.* 2008;107(6):1819–21.
82. Utsunomiya T, Krausz MM, Shepro D, Hechtman HB. Prostaglandin control of plasma and platelet 5-hydroxytryptamine in normal and embolized animals. *Am J Physiol.* 1981;241(5):H766–71.
83. Stratmann G, Gregory GA. Neurogenic and humoral vasoconstriction in acute pulmonary thromboembolism [see comment]. *Anesth Analg.* 2003;97(2):341–54.
84. Huval WV, Mathieson MA, Stemp LI, et al. Therapeutic benefits of 5-hydroxytryptamine inhibition following pulmonary embolism. *Ann Surg.* 1983;197(2):220–5.
85. Said SI. Metabolic functions of the pulmonary circulation. *Circ Res.* 1982;50(3):325–33.
86. Philpot RM, Andersson TB, Eling TE. Uptake, accumulation, and metabolism of chemicals by the lung. In: Bakhle YS, Vane JR, editors. *Metabolic functions of the lung.* New York: Marcel Dekker; 1977. p. 123–71.
87. Garcia JG, Noonan TC, Jubiz W, Malik AB. Leukotrienes and the pulmonary microcirculation. *Am Rev Respir Dis.* 1987;136(1):161–9.
88. Samuelsson B, Dahlen SE, Lindgren JA, Rouzer CA, Serhan CN. Leukotrienes and lipoxins: structures, biosynthesis, and biological effects. *Science.* 1987;237(4819):1171–6.
89. Haeggstrom JZ, Kull F, Rudberg PC, Tholander F, Thunissen MMGM. Leukotriene A4 hydrolase. *Prostaglandins Other Lipid Mediat.* 2002;68–69:495–510.
90. Yang G, Chen G, Wang D. Effects of prostaglandins and leukotrienes on hypoxic pulmonary vasoconstriction in rats. *J Tongji Med Univ.* 2000;20(3):197–9.
91. Caironi P, Ichinose F, Liu R, Jones RC, Bloch KD, Zapol WM. 5-Lipoxygenase deficiency prevents respiratory failure during ventilator-induced lung injury [see comment]. *Am J Respir Crit Care Med.* 2005;172(3):334–43.
92. Leitch AG. The role of leukotrienes in asthma. *Ann Acad Med Singapore.* 1985;14(3):503–7.
93. Sprague RS, Stephenson AH, Dahms TE, Lonigro AJ. Proposed role for leukotrienes in the pathophysiology of multiple systems organ failure. *Crit Care Clin.* 1989;5(2):315–29.
94. Orfanos SE, Mavrommatti I, Korovesi I, Roussos C. Pulmonary endothelium in acute lung injury: from basic science to the critically ill. *Intensive Care Med.* 2004;30(9):1702–14.
95. Huang SK, Peters-Golden M. Eicosanoid lipid mediators in fibrotic lung diseases: ready for prime time? *Chest.* 2008;133(6):1442–50.
96. Del Giudice MM, Pezzullo A, Capristo C, et al. Leukotriene modifiers in the treatment of asthma in children. *Ther Adv Respir Dis.* 2009;3(5):245–51.
97. O'Byrne PM, Gauvreau GM, Murphy DM. Efficacy of leukotriene receptor antagonists and synthesis inhibitors in asthma. *J Allergy Clin Immunol.* 2009;124(3):397–403.
98. Tantisira KG, Drazen JM. Genetics and pharmacogenetics of the leukotriene pathway. *J Allergy Clin Immunol.* 2009;124(3): 422–7.
99. Murphy RC, Gijon MA. Biosynthesis and metabolism of leukotrienes [erratum appears in *Biochem J.* 2007 Sep 15;406(3): 527]. *Biochem J.* 2007;405(3):379–95.
100. Romano M. Lipid mediators: lipoxin and aspirin-triggered 15-epi-lipoxins. *Inflamm Allergy Drug Targets.* 2006;5(2): 81–90.
101. Romano M, Recchia I, Recchiuti A. Lipoxin receptors. *ThescientificWorldJournal.* 2007;7:1393–412.
102. Soyombo O, Spur BW, Lee TH. Effects of lipoxin A4 on chemotaxis and degranulation of human eosinophils stimulated by platelet-activating factor and N-formyl-L-methionyl-L-leucyl-L-phenylalanine. *Allergy.* 1994;49(4):230–4.
103. Raud J, Palmertz U, Dahlen SE, Hedqvist P. Lipoxins inhibit microvascular inflammatory actions of leukotriene B4. *Adv Exp Med Biol.* 1991;314:185–92.
104. Le Y, Li B, Gong W, et al. Novel pathophysiological role of classical chemotactic peptide receptors and their communications with chemokine receptors. *Immunol Rev.* 2000;177:185–94.
105. Colgan SP, Serhan CN, Parkos CA, Delp-Archer C, Madara JL. Lipoxin A4 modulates transmigration of human neutrophils across intestinal epithelial monolayers. *J Clin Invest.* 1993;92(1):75–82.
106. Brezinski ME, Gimbrone Jr MA, Nicolaou KC, Serhan CN. Lipoxins stimulate prostacyclin generation by human endothelial cells. *FEBS Lett.* 1989;245(1–2):167–72.
107. Wenzel SE, Busse WW, The National Heart L, Blood Institute's Severe Asthma Research P. Severe asthma: lessons from the

- Severe Asthma Research Program. *J Allergy Clin Immunol.* 2007;119(1):14–21; quiz 22–13.
108. Vachier I, Bonnans C, Chavis C, et al. Severe asthma is associated with a loss of LX4, an endogenous anti-inflammatory compound. *J Allergy Clin Immunol.* 2005;115(1):55–60.
109. Levy BD, Bonnans C, Silverman ES, et al. Diminished lipoxin biosynthesis in severe asthma. *Am J Respir Crit Care Med.* 2005;172(7):824–30.
110. Kupczyk M, Antczak A, Kuprys-Lipinska I, Kuna P. Lipoxin A4 generation is decreased in aspirin-sensitive patients in lysine-aspirin nasal challenge in vivo model. *Allergy.* 2009;64(12):1746–52.
111. Van Hove CL, Maes T, Joos GF, Tournoy KG. Chronic inflammation in asthma: a contest of persistence vs. resolution. *Allergy.* 2008;63(9):1095–109.
112. Bonnans C, Levy BD. Lipid mediators as agonists for the resolution of acute lung inflammation and injury. *Am J Respir Cell Mol Biol.* 2007;36(2):201–5.
113. Serhan CN. Lipoxins and novel aspirin-triggered 15-epi-lipoxins (ATL): a jungle of cell-cell interactions or a therapeutic opportunity? *Prostaglandins.* 1997;53(2):107–37.
114. Ramalho TC, Rocha MVJ, da Cunha EFF, Freitas MP. The search for new COX-2 inhibitors: a review of 2002–2008 patients. *Expert Opin Ther Pat.* 2009;19(9):1193–228.
115. Grosser T. Variability in the response to cyclooxygenase inhibitors: toward the individualization of nonsteroidal anti-inflammatory drug therapy. *J Investig Med.* 2009;57(6):709–16.
116. Funk CD, FitzGerald GA. COX-2 inhibitors and cardiovascular risk. *J Cardiovasc Pharmacol.* 2007;50(5):470–9.
117. Frangos JA, Eskin SG, McIntire LV, Ives CL. Flow effects on prostacyclin production by cultured human endothelial cells. *Science.* 1985;227(4693):1477–9.
118. Eling TE, Ally AI. Pulmonary biosynthesis and metabolism of prostaglandins and related substances. *Environ Health Perspect.* 1984;55:159–68.
119. Robinson C, Hardy CC, Holgate ST. Pulmonary synthesis, release, and metabolism of prostaglandins. *J Allergy Clin Immunol.* 1985;76(2 Pt 2):265–71.
120. McGiff JC, Terragno NA, Strand JC, Lee JB, Lonigro AJ, Ng KK. Selective passage of prostaglandins across the lung. *Nature.* 1969;223(5207):742–5.
121. Dusting GJ, Moncada S, Vane JR. Recirculation of prostacyclin (PGI2) in the dog. *Br J Pharmacol.* 1978;64(2):315–20.
122. Gardiner PJ. Eicosanoids and airway smooth muscle. *Pharmacol Ther.* 1989;44(1):1–62.
123. Regner KR, Connolly HM, Schaff HV, Albright RC. Acute renal failure after cardiac surgery for carcinoid heart disease: incidence, risk factors, and prognosis. *Am J Kidney Dis.* 2005;45(5):826–32.
124. Zeldin DC, Foley J, Ma J, et al. CYP2J subfamily P450s in the lung: expression, localization, and potential functional significance. *Mol Pharmacol.* 1996;50(5):1111–7.
125. Salvail D, Dumoulin M, Rousseau E. Direct modulation of tracheal Cl⁻ channel activity by 5, 6- and 11, 12-EET. *Am J Physiol.* 1998;275(3 Pt 1):L432–41.
126. Birks EK, Bousamra M, Presberg K, Marsh JA, Effros RM, Jacobs ER. Human pulmonary arteries dilate to 20-HETE, an endogenous eicosanoid of lung tissue. *Am J Physiol.* 1997;272 (5 Pt 1):L823–9.
127. Jacobs ER, Zeldin DC. The lung HETEs (and EETs) up. *Am J Physiol Heart Circ Physiol.* 2001;280(1):H1–10.
128. Sirois P, Gutkowska J. Atrial natriuretic factor immunoreactivity in human fetal lung tissue and perfusates. *Hypertension.* 1988;11(2 Pt 2):I62–5.
129. Di Nardo P, Peruzzi G. Physiology and pathophysiology of atrial natriuretic factor in lungs. *Can J Cardiol.* 1992;8(5):503–8.
130. Turrin M, Gillis CN. Removal of atrial natriuretic peptide by perfused rabbit lungs in situ. *Biochem Biophys Res Commun.* 1986;140(3):868–73.
131. Tomlinson JW, Walker EA, Bujalska IJ, et al. 11beta-hydroxysteroid dehydrogenase type 1: a tissue-specific regulator of glucocorticoid response. *Endocr Rev.* 2004;25(5):831–66.
132. Garbrecht MR, Klein JM, Schmidt TJ, Snyder JM. Glucocorticoid metabolism in the human fetal lung: implications for lung development and the pulmonary surfactant system. *Biol Neonate.* 2006;89(2):109–19.
133. Baker RW, Walker BR, Shaw RJ, et al. Increased cortisol: cortisone ratio in acute pulmonary tuberculosis. *Am J Respir Crit Care Med.* 2000;162(5):1641–7.
134. Huang CH, Huang HH, Chen TL, Wang MJ. Perioperative changes of plasma endothelin-1 concentrations in patients undergoing cardiac valve surgery. *Anaesth Intensive Care.* 1996;24(3):342–7.
135. Dupuis J, Cernacek P, Tardif JC, et al. Reduced pulmonary clearance of endothelin-1 in pulmonary hypertension. *Am Heart J.* 1998;135(4):614–20.
136. Drinker CK, Churchill ED, Ferry RM. The volume of blood in the heart and lungs. *Am J Physiol.* 1926;(Ixxvii):590–622.
137. Campbell I, Waterhouse J. Fluid balance and non-respiratory functions of the lung. *Anaesth Intensive Care Med.* 2005; 6(11):370–1.
138. Cotter G, Metra M, Milo-Cotter O, Dittrich HC, Gheorghiade M. Fluid overload in acute heart failure – re-distribution and other mechanisms beyond fluid accumulation. *Eur J Heart Fail.* 2008;10(2):165–9.
139. Jules-Elysee K, Blanck TJ, Catravas JD, et al. Angiotensin-converting enzyme activity: a novel way of assessing pulmonary changes during total knee arthroplasty. *Anesth Analg.* 2004;99(4):1018–23.
140. Lovering AT, Stickland MK, Kelso AJ, Eldridge MW. Direct demonstration of 25- and 50-microm arteriovenous pathways in healthy human and baboon lungs. *Am J Physiol Heart Circ Physiol.* 2007;292(4):H1777–81.
141. Lovering AT, Haverkamp HC, Romer LM, Hokanson JS, Eldridge MW. Transpulmonary passage of 99mTc macroaggregated albumin in healthy humans at rest and during maximal exercise. *J Appl Physiol.* 2009;106(6):1986–92.
142. Abrams GA, Rose K, Fallon MB, et al. Hepatopulmonary syndrome and venous emboli causing intracerebral hemorrhages after liver transplantation: a case report. *Transplantation.* 1999;68(11):1809–11.
143. Colohan AR, Perkins NA, Bedford RF, Jane JA. Intravenous fluid loading as prophylaxis for paradoxical air embolism. *J Neurosurg.* 1985;62(6):839–42.
144. Breeze RG, Wheeldon EB. The cells of the pulmonary airways. *Am Rev Respir Dis.* 1977;116(4):705–77.
145. Rogers DF. The airway goblet cell. *Int J Biochem Cell Biol.* 2003;35(1):1–6.
146. Huffmyer JL, Littlewood KE, Nemergut EC. Perioperative management of the adult with cystic fibrosis. *Anesth Analg.* 2009;109(6):1949–61.

147. Nadel JA. Neural control of airway submucosal gland secretion. *Eur J Respir Dis Suppl.* 1983;128(Pt 1):322–6.
148. Reid L. Measurement of the bronchial mucous gland layer: a diagnostic yardstick in chronic bronchitis. *Thorax.* 1960;15: 132–41.
149. Gallagher JT, Kent PW, Passatore M, Phipps RJ, Richardson PS. The composition of tracheal mucus and the nervous control of its secretion in the cat. *Proceedings of the Royal Society of London. Dec 31 1975;Series B, Containing Papers of a Biological Character.* 1975;192(1106):49–76.
150. Heidsiek JG, Hyde DM, Plopper CG, St George JA. Quantitative histochemistry of mucusubstance in tracheal epithelium of the macaque monkey. *J Histochem Cytochem.* 1987;35(4):435–42.
151. Evans CM, Williams OW, Tuvim MJ, et al. Mucin is produced by clara cells in the proximal airways of antigen-challenged mice. *Am J Respir Cell Mol Biol.* 2004;31(4):382–94.
152. Boers JE, Amberg AW, Thunnissen FB. Number and proliferation of clara cells in normal human airway epithelium. *Am J Respir Crit Care Med.* 1999;159(5 Pt 1):1585–91.
153. Reynolds SD, Malkinson AM. Clara cell: progenitor for the bronchiolar epithelium. *Int J Biochem Cell Biol.* 2009;42(1):1–4.
154. Krishnaswamy G, Ajitawi O, Chi DS. The human mast cell: an overview. *Methods Mol Biol.* 2006;315:13–34.
155. Taube C, Stassen M. Mast cells and mast cell-derived factors in the regulation of allergic sensitization. *Chem Immunol Allergy.* 2008;94:58–66.
156. Peters A, Veronesi B, Calderon-Garciduenas L, et al. Translocation and potential neurological effects of fine and ultrafine particles a critical update. Part Fibre Toxicol [Electronic Resource]. 2006;3:13.
157. Jakubzick C, Tacke F, Llodra J, van Rooijen N, Randolph GJ. Modulation of dendritic cell trafficking to and from the airways. *J Immunol.* 2006;176(6):3578–84.
158. Matthay MA, Folkesson HG, Clerici C. Lung epithelial fluid transport and the resolution of pulmonary edema. *Physiol Rev.* 2002;82(3):569–600.
159. Matthay MA, Clerici C, Saumon G. Invited review: active fluid clearance from the distal air spaces of the lung. *J Appl Physiol.* 2002;93(4):1533–41.
160. Andreeva AV, Kutuzov MA, Voyno-Yasenetskaya TA. Regulation of surfactant secretion in alveolar type II cells. *Am J Physiol Lung Cell Mol Physiol.* 2007;293(2):L259–71.
161. Weaver TE, Conkright JJ. Function of surfactant proteins B and C. *Annu Rev Physiol.* 2001;63:555–78.
162. Wanner A, Salathe M, O’Riordan TG. Mucociliary clearance in the airways. *Am J Respir Crit Care Med.* 1996;154(6 Pt 1): 1868–902.
163. Boucher RC. Evidence for airway surface dehydration as the initiating event in CF airway disease. *J Intern Med.* 2007;261(1): 5–16.
164. McFadden Jr ER. Heat and water exchange in human airways. *Am Rev Respir Dis.* 1992;146(5 Pt 2):S8–10.
165. Crouch E, Wright JR. Surfactant proteins a and d and pulmonary host defense. *Annu Rev Physiol.* 2001;63:521–54.
166. Wu H, Kuzmenko A, Wan S, et al. Surfactant proteins A and D inhibit the growth of Gram-negative bacteria by increasing membrane permeability [see comment]. *J Clin Invest.* 2003; 111(10):1589–602.
167. Wright JR. Pulmonary surfactant: a front line of lung host defense [comment]. *J Clin Invest.* 2003;111(10):1453–5.

Pharmacology of the Airways

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Key Points

- Short-acting beta-2 adrenergic agonists are administered for the acute relief of bronchospasm, wheezing, and airflow obstruction. Long-acting beta-2 adrenergic agonists are for long-term control of symptoms.
- Inhaled anticholinergics are first-line therapy in COPD. They are useful for both maintenance therapy and in acute exacerbations.
- Inhaled corticosteroids are used to control inflammation in asthma and COPD. In asthma, they can be used as monotherapy. In COPD, they are used in conjunction with long-acting beta-adrenergic agonists.
- Systemic corticosteroids are used for the reduction of inflammation in asthma and COPD exacerbations and are not typically prescribed as maintenance therapy.
- Leukotriene modifiers, mast cell stabilizers, and methylxanthines are alternative therapies used in asthma when symptoms are not well-controlled on first-line therapy.
- Volatile and intravenous anesthetics provide a degree of bronchodilation that may be useful in treating intraoperative bronchoconstriction.
- Helium/oxygen mixtures, antihistamines, and magnesium sulfate are alternative therapies used when bronchospasm does not respond to conventional therapies.

Introduction

This chapter reviews the pharmacology of agents commonly encountered in anesthetic practice that are either administered to treat pulmonary diseases or administered into the airway for action at end organs other than the lung but have effects on the airway. Drugs that modify the state of the autonomic nervous system (ANS) and the airway will be reviewed along with medications that modify or suppress inflammation of the airway. Lastly, the action of anesthetic agents on the airway will be reviewed along with the actions of several adjunctive agents.

Pharmacologic agents administered via the lungs take advantage of the unique interface between air and blood allowing for rapid uptake of drugs into the bloodstream or immediate utilization by cells that populate the airway. The delivery of medications to the lungs can have systemic effects, direct effects on the airway, or both. For example, inhaled anesthetics are delivered via the lungs to act in the brain, and have bronchodilatory effects. Conversely, beta-adrenergic agonists delivered via aerosol exert direct effects on bronchial smooth muscle with few systemic effects. Drugs administered to the airway take advantage of the rapid exposure to blood and pulmonary parenchymal cells making them advantageous for treating pulmonary parenchymal diseases such as asthma and chronic obstructive pulmonary disease (COPD).

Influence of the Autonomic Nervous System on the Airway and Modulation of the Response

Traditionally, the ANS has been divided into two major parts, the parasympathetic and sympathetic nervous systems. The parasympathetic nervous system regulates airway caliber, airway glandular activity, and airway microvasculature [1–4]. The vagus nerve provides the preganglionic fibers which synapse with postganglionic fibers in airway parasympathetic ganglia [1–4]. Acetylcholine activates the muscarinic (M3) receptor of postganglionic fibers of the parasympathetic nervous system to produce bronchoconstriction [5]. Anticholinergics can provide bronchodilation even in the resting state since the parasympathetic nervous system produces a basal level of resting bronchomotor tone [3, 4, 6].

Although the sympathetic nervous system plays no direct role in control of airway muscle tone, beta-2 adrenergic receptors are present on airway smooth muscle cells and cause bronchodilation via G-stimulatory mechanisms [1–5]. The abundance of these receptors in the airway allows for pharmacologic manipulation of airway tone [7].

The ANS also influences bronchomotor tone through the nonadrenergic noncholinergic (NANC) system [2, 4, 8, 9]. The exact role of NANC in humans is not well defined; it has excitatory and inhibitory neuropeptides that influence inflammation and smooth muscle tone, respectively [2, 8]. Vasoactive intestinal peptide (VIP) and nitric oxide (NO) are the main inhibitory transmitters thought to be responsible for airway smooth muscle relaxation [2, 8]. Substance P (SP) and neurokinin A (NKA) are the main excitatory transmitters and have been shown to cause neurogenic inflammation, including bronchoconstriction [2, 8]. The precise role of NANC in healthy and diseased human lung is unclear. Further study is needed to fully elucidate the role that this group of neuropeptides has in the regulation of bronchial smooth muscle responsiveness.

Inhaled Adrenergic Agonists

The mainstay of therapy for bronchospasm, wheezing, and airflow obstruction is beta-adrenergic agonists. Beta-adrenergic

agonists used in clinical practice are typically delivered via inhalers or nebulizers, are beta-2 selective, and are divided into short- and long-acting therapies [10]. Short-acting beta-2 agonist therapy is effective for the rapid relief of wheezing, bronchospasm, and airflow obstruction [10]. Longer-acting beta-2 agonists are used as maintenance therapy providing improvement in lung function and reduction in symptoms and exacerbations [10]. Please refer to Table 8.1 for beta-2 selective agonists that play a prominent role in the management of airway diseases and symptoms both in and out of the operating room.

Mechanism of Action

Short-acting beta-2 agonists bind to the beta-2 adrenergic receptor located on the plasma membrane of smooth muscle cells, epithelial, endothelial, and many other types of airway cells [7, 11]. Figure 8.1 demonstrates how a ligand binding to the receptor causes a G-stimulatory protein to activate adenylate cyclase-converting adenosine triphosphate (ATP) into cyclic adenosine monophosphate (cAMP) [7, 11]. It is unknown precisely how cAMP causes smooth muscle relaxation; however, decreases in calcium release and alterations in membrane potential are the most likely mechanisms [7]. Longer-acting beta-2 agonists have the same mechanism of action as short-acting beta-2 agonists; however, they have unique properties that allow for a longer duration of action. For example, salmeterol has a longer duration of action because a side chain binds to the beta-2 receptor and prolongs the activation of the receptor [11, 12]. The lipophilic side chain of formoterol allows for interaction with the lipid bilayer of the plasma membrane and a slow, steady release prolonging its duration of action [11].

Clinical Applications

Beta-2 agonists have a central role in the management of obstructive airway diseases allowing for control of symptoms and improvement in lung function. Short-acting beta-2 agonists such as albuterol, levalbuterol, metaproterenol, and pirbuterol are prescribed for the rapid relief of wheezing, bronchospasm, and airflow obstruction [10]. Clinical effect is seen in a matter of minutes and lasts up to 4–6 h [11]. Scheduled, daily use of

TABLE 8.1. Pharmacologic influence on the autonomic nervous system.

Systemic adrenergic agonists	Inhaled adrenergic agonists	Inhaled cholinergic antagonists	Systemic cholinergic antagonists
Terbutaline	Short-acting Albuterol Levalbuterol	Short-acting Ipratropium	Atropine
Epinephrine	Metaproterenol		Scopolamine
Albuterol	Pirbuterol		Glycopyrrolate
	Long-acting Salmeterol	Long-acting Tiotropium	
	Formoterol		
	Arformoterol		

Adapted from Fanta et al. [10]

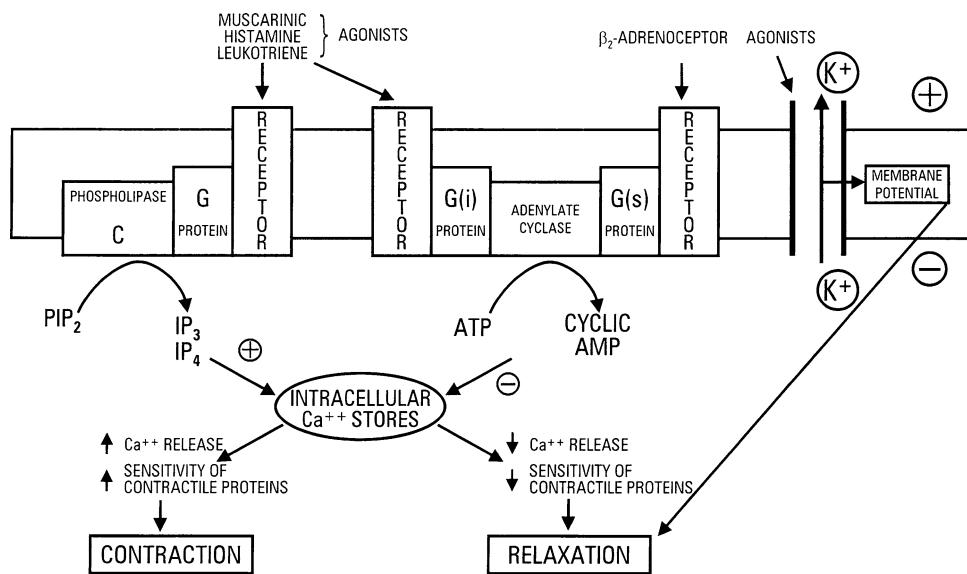


FIG. 8.1. Effects of agonists at the beta-2 receptor and at the muscarinic receptor. Stimulation of the beta-2 receptor will cause a decrease in calcium release and relaxation of smooth muscle. Blockade of the muscarinic receptor will prevent the release of calcium and smooth muscle contraction. ATP adenosine triphosphate; AMP adenosine monophosphate; IP Inositol phosphate; PIP₂ phosphoinositide bisphosphate (reprinted with permission of the Thoracic Society. Copyright© American Thoracic Society. Johnson [7]. Official Journal of the American Thoracic Society).

short-acting beta-2 agonists has largely fallen out of favor and they are now used primarily as rescue therapy [13–15]. Long-acting beta-2 agonists are prescribed for control of symptoms when rescue therapies (i.e., short-acting beta-2 agonists) are used greater than two times per week [10, 16]. Combination therapy including a long-acting beta-2 agonist and an inhaled corticosteroid (IC) are effective in reducing symptoms, reducing the risk of exacerbation, and improving lung function while minimizing the dose of IC [10, 17].

Side Effects

Systemic absorption of inhaled beta-2 agonists is responsible for a myriad of side effects, most of which are not serious. Most commonly, beta-2 agonist therapy leads to tremors and tachycardia secondary to direct stimulation of the beta-2 adrenergic receptor in skeletal muscle or vasculature, respectively [10, 11, 18, 19]. In severe asthma, beta-2 agonists may cause a temporary reduction in arterial oxygen tension of 5 mmHg or more secondary to beta-2-mediated vasodilation in poorly ventilated lung regions [11, 20]. Hyperglycemia, hypokalemia, and hypomagnesemia also can occur with beta-2 agonist therapy but the severity of these side effects tends to diminish with regular use [11]. Tolerance to beta-2 agonists can occur with regular use over a period of weeks, and, while not affecting peak bronchodilation, can be evidenced by a decrease in the duration of bronchodilation and the magnitude of side effects (tremor, tachycardia, etc.) [11, 21, 22]. Tolerance likely reflects beta-2 adrenergic receptor down-regulation [11]. Last, beta-2 agonist therapy

withdrawal after regular use can produce transient bronchial hyperresponsiveness [11].

Safety Concerns

Recent evidence has associated the use of long-acting beta-2 agonist therapy without concomitant use of a steroid inhaler with fatal and near-fatal asthma attacks [10, 23]. In light of this evidence it seems prudent to save long-acting beta-2 agonists for patients that are poorly controlled on inhaled steroids alone or for those patients with symptoms sufficiently challenging to warrant the potential extra risk associated with use of the agents [10, 23].

Systemic Adrenergic Agonists

Systemic administration of adrenergic agonists for asthma was used more frequently in the past. Oral, intravenous, or subcutaneous administration of beta-specific or nonspecific adrenergic agonists is now reserved for rescue therapy.

Mechanism of Action

The mechanism of action of systemically administered adrenergic agonists is the same as it is for inhaled agents. Binding of the drug to the beta-2 adrenergic receptor on smooth muscle cells in the airway is responsible for the bronchodilatory effects [7]. Specifically, beta-2 receptor stimulation induces a G-stimulatory protein to convert ATP to cAMP and in turn reduces intracellular calcium release and alters membrane potential [7, 11].

Clinical Applications

Terbutaline can be given orally, subcutaneously, or intravenously (IV), albuterol (salbutamol) can be given intravenously, and epinephrine is usually given subcutaneously or intravenously. Regardless of the route of administration, all three will produce bronchodilation. Comparison of intravenous and inhaled formulations of terbutaline failed to demonstrate any difference in bronchodilation and, with the propensity for IV formulations to cause side effects, inhaled therapy should be considered the first-line treatment [24, 25]. This principle not only applies to terbutaline but also to all beta-adrenergic agonists that are available in IV and inhaled forms [16]. If inhaled therapy is not readily available or if inhaled therapy is maximized and symptoms persist, then subcutaneous epinephrine or terbutaline can be administered with improvement in symptoms and spirometry values [26]. In summary, subcutaneous or IV beta agonists should be reserved only for rescue therapy.

Side Effects

The side-effect profile of systemic adrenergic agonists is similar to that for inhalational adrenergic agonists. The most common side effects are tremor and tachycardia [10, 11]. Arterial oxygen tension can be transiently decreased and hyperglycemia, hypokalemia, and hypomagnesemia can also be present [10, 11]. Escalating oral, subcutaneous, or IV doses can be associated with a greater incidence of side effects for the same degree of bronchodilation compared to inhaled beta-adrenergic agonists [10, 11].

Inhaled Cholinergic Antagonists

The use of anticholinergics for maintenance therapy and treatment of acute exacerbations in obstructive airway diseases is common. The parasympathetic nervous system is primarily responsible for bronchomotor tone and inhaled anticholinergics act on muscarinic receptors in the airway to reduce tone [2]. The use of inhaled anticholinergics (see Table 8.1) in COPD as maintenance and rescue therapy is considered first-line, standard treatment [27]. Anticholinergics are not used for maintenance therapy in asthma and are only recommended for use in acute exacerbations [10, 16, 27, 28].

Mechanism of Action

The targets of therapy for anticholinergics are the muscarinic receptors located in the airway. There are three subtypes of muscarinic receptors found in the human airway [29]. Muscarinic 2 (M2) is present on postganglionic cells and is responsible for limiting production of acetylcholine and protects against bronchoconstriction [29]. M2 is not the target of inhaled anticholinergics but is antagonized by them [29]. Muscarinic 1(M1) and muscarinic 3 (M3) receptors are responsible for bronchoconstriction and mucus production

and are the targets of inhaled anticholinergic therapy [29]. Acetylcholine binds to the M3 and M1 receptors and causes smooth muscle contraction (see Fig. 8.1) via increases in cyclic guanosine monophosphate (cGMP) or by activation of a G protein (Gq) [5, 6, 29]. Gq activates phospholipase C to produce inositol triphosphate (IP3), which causes release of calcium from intracellular stores and activation of myosin light chain kinase causing smooth muscle contraction [5, 6, 29]. Anticholinergics inhibit this cascade and reduce smooth muscle tone by decreasing release of calcium from intracellular stores [5, 6].

Clinical Applications

There are two inhaled anticholinergics specifically approved for the treatment of obstructive airway diseases. Ipratropium is classified as a short-acting anticholinergic and is commonly used as maintenance therapy for COPD and as rescue therapy for both COPD and asthmatic exacerbations [27, 29]. It is not indicated for the routine management of asthma [10, 16, 27, 28]. Patients treated with ipratropium experience an increase in exercise tolerance, decrease in dyspnea, and improved gas exchange [29]. Tiotropium is the only long-acting anticholinergic available for COPD maintenance therapy. Tiotropium has been shown to reduce COPD exacerbations, respiratory failure, and all-cause mortality [30].

Side Effects

Inhaled anticholinergics are poorly absorbed and therefore serious side effects are uncommon. Most commonly, patients experience dry mouth, urinary retention, and can experience pupillary dilation and blurred vision if the eyes are inadvertently exposed to the drug [29]. Some initial data suggested an increase in cardiovascular and stroke complications with tiotropium, however additional studies did not consistently demonstrate these complications [29]. In general, anticholinergics are safe and effective treatment for patients with obstructive airway diseases.

Systemic Cholinergic Antagonists

The systemically administered anticholinergics atropine and glycopyrrrolate act via the same mechanisms as inhaled anticholinergics. While these anticholinergics can be administered by IV or inhalation, significant systemic absorption occurs and their use is generally limited by side effects. Atropine, in particular, is limited in use because of its tertiary ammonium structure [27]. It has a tendency to cause tachycardia, gastrointestinal upset, blurred vision, dry mouth, and central nervous system effects secondary to its ability to cross the blood-brain barrier [27]. Glycopyrrrolate has a quaternary ammonium structure and is insoluble in lipids, similar to ipratropium and tiotropium, and has fewer systemic side effects than atropine [27, 29]. Intravenous glycopyrrrolate is also clinically limited in use secondary to side

effects [31]. Glycopyrrolate has been studied as inhaled therapy, however, and is an effective bronchodilator with an intermediate duration of action [32–35]. Clinically, it has never been popular as a mainstay of therapy for obstructive airway diseases.

Influence of Inflammation on the Airway and Modulation of the Response

Asthma and COPD, the most common obstructive airway diseases, have a component of inflammation as part of their pathogenesis. Although inflammation is a common pathogenesis, the characteristics and prominent cellular elements involved in the inflammatory process for each disease are distinct [36]. In COPD, neutrophils, macrophages, CD8+ T lymphocytes, and eosinophils are more prominent in the inflammatory composition [36]. In asthma, eosinophils play a more prominent role followed by mast cells, CD4+ T lymphocytes, and macrophages in the inflammatory composition [36]. Inflammatory cell types present in sputum, biopsy specimens, and bronchoalveolar lavage fluid can help predict the response to anti-inflammatory therapy [36]. For example, eosinophilia in induced sputum of a patient presenting with a COPD exacerbation predicts an increase in steroid responsiveness [36–38]. Patients presenting to the operating room with obstructive airway diseases have a high likelihood of being prescribed and taking or being exposed to one of the anti-inflammatory therapies in Table 8.2 for control of their disease.

Inhaled Corticosteroids

In the treatment of asthma, the use of ICs reduces the inflammatory changes associated with the disease, thereby improving lung function and reducing exacerbations that result in hospitalization and death [10, 39–41]. On the contrary, the use of ICS as monotherapy in COPD is discouraged [29]. In COPD, ICs are used as a part of combination therapy along

with long-acting beta-adrenergic agonists (LABA). The combination of drugs acts synergistically and is useful for reducing inflammation [29]. Currently, combination therapy of ICS and LABA is recommended for use in severe to very severe COPD [29, 42].

Mechanism of Action

The glucocorticoid receptor alpha (GR α) located in the cytoplasm of airway epithelial cells is the primary target of ICs [43, 44]. Passive diffusion of steroids into the cell allows for binding of the steroid ligand to GR α , dissociation of heat shock proteins, and subsequent translocation to the nucleus [44]. Figure 8.2 shows how the steroid–receptor complex can have a multitude of actions when it enters the nucleus [44]. The complex can bind to promoter regions of DNA sequences and either induce or suppress gene expression [44]. Additionally, the steroid–receptor complex can interact with transcription factors already in place, such as the ones responsible for proinflammatory mediators, without binding to DNA and repress expression of those genes [43, 44]. The steroid–receptor complex also can affect chromatin structure by association with transcription factors that influence the winding of DNA around histones, reducing access of RNA polymerase and other transcription factors, and thus reducing expression of inflammatory gene products [43, 44].

Clinical Applications

ICs are used in asthma as part of a multimodal treatment regimen and are added to a therapeutic regimen when there is an increase in severity or frequency of asthma exacerbations [10]. There is good evidence to show that ICS can reduce both hospitalizations and death in asthma [40, 41]. The use of ICS in COPD is limited to use in severe to very severe COPD and in combination with LABA [29]. Although no improvement in mortality has been consistently demonstrated with combination therapy (ICS/LABA), there are reported improvements in health status and lung function along with a reduction in exacerbations [29, 42].

Side Effects and Safety Concerns

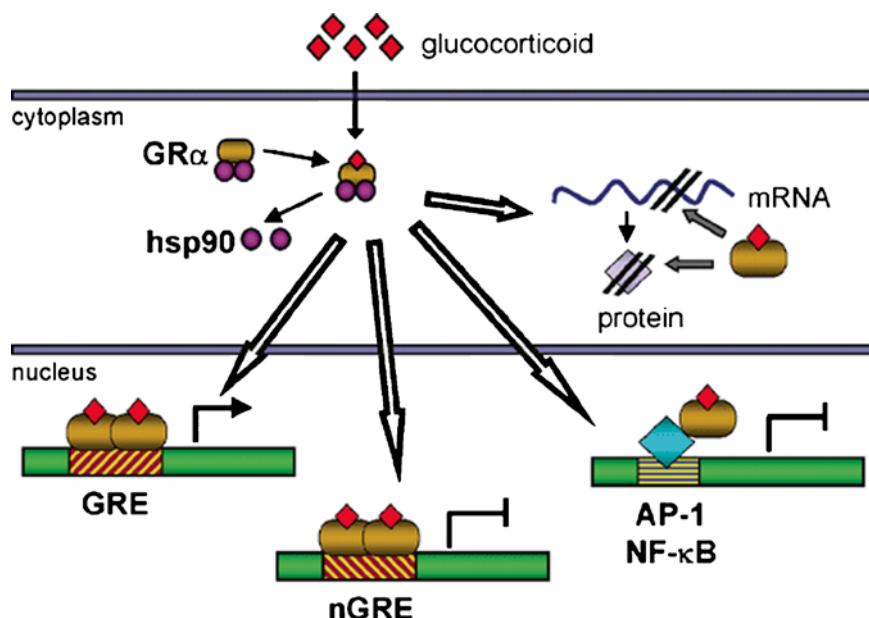
Side effects have been reported with the use of ICS in asthma and COPD. A recent meta-analysis reported an increase in pneumonia and serious pneumonia but not pneumonia-related deaths when ICS was used in the treatment of COPD [45]. Other reported side effects in COPD and asthma include oropharyngeal candidiasis, pharyngitis, easy bruising, osteoporosis, cataracts, elevated intraocular pressure, dysphonia, cough, and growth retardation in children [10, 29, 42]. As with any pharmacotherapy, the risks and benefits of therapy must be weighed, and the patient must be carefully monitored for adverse effects. This is especially true with the use of ICS in obstructive lung diseases.

TABLE 8.2. Pharmacologic influence on inflammation.

Inhaled corticosteroids	Leukotriene modifiers	Mast cell stabilizers	Methylxanthines
Monotherapy	Antagonists		
Beclomethasone	Montelukast	Cromolyn sodium	Theophylline
Budesonide	Zafirlukast	Nedocromil	Aminophylline
Ciclesonide	Pranlukast (not in U.S.)		
Flunisolide			
Fluticasone	Inhibitors		
Mometasone	Zileuton		
Triamcinolone			
Combination therapy			
Budesonide/Formoterol			
Fluticasone/Salmeterol			

Adapted from Fanta et al. [10]

FIG. 8.2. Action of glucocorticoids. Glucocorticoids can bind to promoter regions inducing or repressing gene expression, act on promoters with transcription factors in place, or influence the structure of chromatin. *GR α* glucocorticoid receptor alpha; *hsp90* heat shock proteins; *mRNA* messenger ribonucleic acid; *GRE* glucocorticoid responsive elements; *nGRE* negative glucocorticoid responsive elements; *NF- κ B* nuclear factor kappa beta; *AP-1* activator protein-1 (reprinted from Pujols et al. [44] with permission).



Systemic Corticosteroids

Systemic corticosteroids given in intravenous or oral form are used for treatment of asthma and COPD exacerbations. The mechanism of action is the same as it is for ICs, activation or suppression of gene products at a transcriptional level and alteration of chromatin structure [43, 44]. Patients that are hospitalized with a COPD exacerbation will typically receive IV corticosteroids to suppress any inflammatory component that may be contributing to the flare up. A study done at the Veterans Affairs medical centers in the United States published in 1999 reported that corticosteroid therapy shortened hospital length of stay and improved forced expiratory volume in 1 s vs. placebo [46]. The study also compared a 2-week regimen vs. an 8 week regimen of corticosteroids and found no difference, concluding that the duration of therapy should last only 2 weeks [46]. In asthma, corticosteroids are recommended for exacerbations that are either severe, with a peak expiratory flow of less than 40% of baseline, or a mild to moderate exacerbation with no immediate response to short-acting beta-adrenergic agonists [16]. The recommended duration of therapy is 3–10 days without tapering [16]. Alternatively, some patients with asthma and COPD will be receiving long-term oral corticosteroid therapy because their disease is difficult to manage. Side effects of systemic corticosteroids are well described and numerous. Hypertension, hyperglycemia, adrenal suppression, increased infections, cataracts, dermal thinning, psychosis, and peptic ulcers are reported complications of corticosteroid therapy [47].

Leukotriene Modifiers

Leukotriene modifiers are used for the treatment of asthma. They are prescribed primarily for long-term control in addition to short-acting beta-adrenergic agonists or in conjunction

with ICs and short-acting beta agonists. Leukotriene modifiers are taken by mouth, produce bronchodilatation in hours, and have maximal effect within days of administration [10]. Their role in the management of COPD is not defined. Future investigations will need to focus on the role these medications can play in the outpatient management of COPD [48].

Mechanism of Action

Arachidonic acid is converted to leukotrienes via the 5-lipoxygenase pathway [49]. Leukotrienes C₄, D₄, and E₄ are the end products of the pathway and cause bronchoconstriction, tissue edema, migration of eosinophils, and increased airway secretions [49]. Leukotriene modifiers come in two different varieties, leukotriene receptor antagonists and leukotriene inhibitors [10]. Figure 8.3 shows how the binding of leukotrienes C₄, D₄, and E₄ at the type 1 cysteinyl leukotriene receptor is blocked by the leukotriene receptor antagonists montelukast, zafirlukast, and pranlukast (not available in the U.S.) [10, 49]. The leukotriene inhibitor zileuton antagonizes 5-lipoxygenase (Fig. 8.3), inhibiting the production of cysteinyl leukotrienes [10, 49].

Clinical Applications

Leukotriene modifiers improve lung function, reduce exacerbations, and are used as long-term asthma therapy [10, 16, 50, 51]. Clinical trials have reported that ICs are superior to leukotriene modifiers for long-term control and should be the first-line choice [16, 52, 53]. Leukotriene modifiers provide an additional pharmacologic option for the control of asthma. Addition of leukotriene modifiers to ICs will improve control of symptoms of asthma as opposed to ICs alone [54].

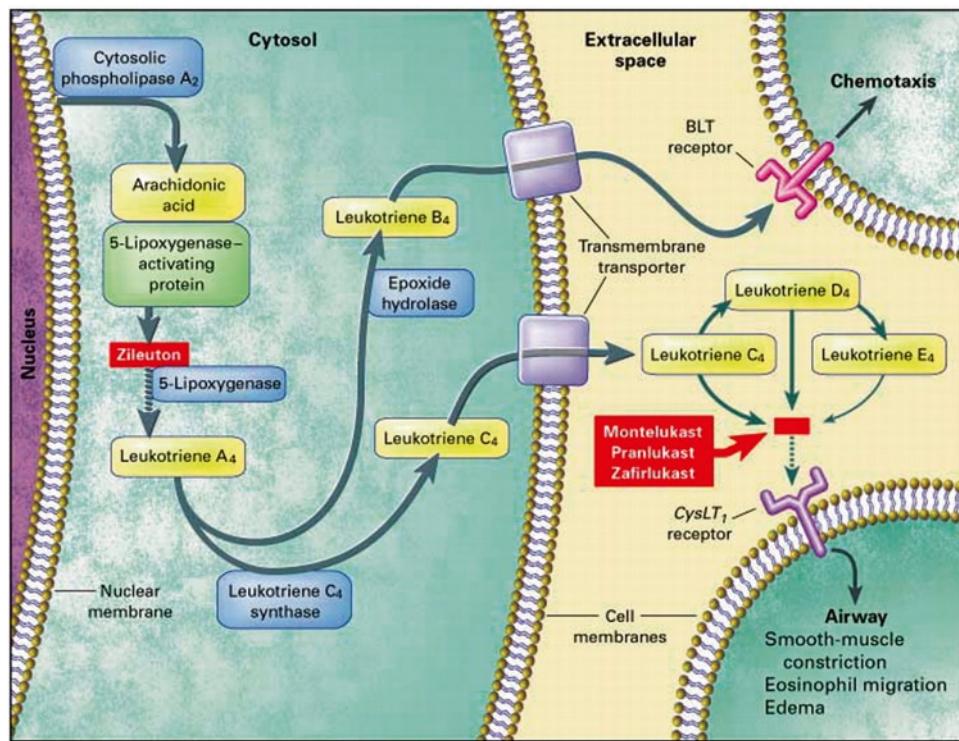


FIG. 8.3. Generation of leukotrienes and action of leukotriene modifying drugs. Leukotriene antagonists block the action of leukotrienes at the cysteinyl leukotriene receptor (CysLT₁) and leukotriene inhibitors block the conversion of arachidonic acid to leukotriene A₄. BLT leukotriene receptor B (reprinted from Drazen et al. [49] with permission, © 1999 Massachusetts Medical Society. All Rights Reserved.).

Side Effects

Overall, leukotriene antagonists are well-tolerated without significant side effects. Links between Churg-Strauss syndrome and the use of leukotriene antagonists have been reported, but it is not clear whether these reports reflect unmasking of a preexisting condition or whether there is a direct link between the two [10, 49]. Zileuton is known to cause a reversible hepatitis in 2–4% of patients [10]. Liver function tests should be checked frequently at first and periodically thereafter to monitor for hepatocellular damage [10, 49].

Mast Cell Stabilizers

Cromolyn sodium and nedocromil are the two prototypical agents in this category that are used in the treatment of asthma. These agents are delivered by powder inhaler and are not first-line therapy for asthma. They do provide an alternative treatment when the control of asthma is not optimal on other conventional therapies [16].

Mechanism of Action

Cromolyn sodium and nedocromil stabilize submucosal and intraluminal mast cells [16, 55]. These drugs interfere with the antigen-dependent release of mediators, such as

histamine and slow-reacting substance of anaphylaxis, that cause bronchoconstriction, mucosal edema, and increased mucus secretion [55].

Clinical Applications

Large systematic reviews of the available literature and consensus statements favor the use of ICS over cromolyn sodium or nedocromil as first-line agents to control symptoms of asthma [16, 56]. Alternatively, cromolyn sodium and nedocromil may be used as preventative treatment before exercise or known allergen exposure causing symptoms of asthma [16].

Side Effects

There are no major side effects reported with the use of cromolyn sodium and nedocromil. The most commonly reported side effects are gastrointestinal upset and coughing or irritation of the throat [55].

Methylxanthines

The role of theophylline, a prototypical methylxanthine, has changed since the introduction of ICS and LABA. Theophylline was a common choice for the control of asthma and COPD because of its bronchodilatory and anti-inflammatory

effects [57]. Currently, theophylline is recommended only as an alternative therapy and is not a first-line choice for asthma or COPD [16, 58, 59].

Mechanism of Action

Theophylline is thought to act via multiple pathways causing improvement in symptoms in obstructive lung diseases. Theophylline is a nonselective inhibitor of phosphodiesterase and increases levels of cyclic AMP and GMP causing smooth muscle relaxation [57]. Antagonism of the A₁ and A₂ adenosine receptors also causes smooth muscle relaxation via inhibition of the release of histamine and leukotrienes from mast cells, another reported action of theophylline [57]. In asthma, theophylline reduces the number of eosinophils in bronchial specimens and, in COPD, reduces the number of neutrophils in sputum, having an anti-inflammatory effect in both conditions [57]. In addition, theophylline activates histone deacetylase and reduces the expression of inflammatory genes [57]. Theophylline and aminophylline are reported to improve diaphragmatic function; however data have not demonstrated this effect consistently [57, 60].

Clinical Applications

Theophylline has been relegated to an alternative therapy in both asthma and COPD. This has occurred largely because of its significant side-effect profile and the subsequent need for monitoring of blood levels [16, 57–59]. Patients that are already on an ICS and a LABA and still have symptoms may benefit from the addition of theophylline, especially if leukotriene modifiers and other alternatives are not tolerated [16, 58, 59].

Side Effects

Theophylline can cause significant and life-threatening side effects if not dosed carefully and monitored appropriately. Side effects tend to be more prominent when blood levels exceed 20 mg/L [57]. The most common side effects include headache, nausea, vomiting, restlessness, abdominal discomfort, gastroesophageal reflux, and diuresis [57]. The most significant side effects include seizures, cardiac arrhythmias, and death [57]. Adverse effects from theophylline may be avoided if the clinician follows the patient carefully, monitors blood levels regularly, and educates the patient on the signs and symptoms of overdose.

Influence of Anesthetics on the Airway

Volatile Anesthetics

Volatile anesthetics have a host of effects on the respiratory system. Volatile anesthetics reduce bronchomotor tone. All commonly used volatile anesthetics (see Table 8.3), except desflurane,

TABLE 8.3. Anesthetics with a favorable influence on bronchomotor tone.

Volatile anesthetics ^a	Intravenous anesthetics ^b
Isoflurane	Propofol
Sevoflurane	Ketamine
Halothane	Midazolam

^aAdapted from Rooke et al. [62]

^bAdapted from Cheng et al. [69]

produce a degree of bronchodilatation that may be helpful in patients with obstructive lung disease or in patients that experience any degree of bronchoconstriction [61, 62]. Rooke and colleagues in 1997 reported that sevoflurane produced a greater reduction in respiratory system resistance than isoflurane or halothane 10 min after the induction of anesthesia [62].

Mechanism of Action

The precise mechanisms by which volatile anesthetics induce bronchodilatation are not completely clear. Animal studies suggest that volatile anesthetics inhibit tracheal smooth muscle contraction by decreasing intracellular calcium, mediated by an increase in intracellular cAMP and by suppression of protein kinase C which, in the absence of volatile anesthetics, sensitizes contractile elements to calcium and inhibits myosin light chain phosphatase [63]. The effect is seen to a greater degree in distal airway smooth muscle secondary to the T-type voltage-dependent calcium channel, which is sensitive to volatile anesthetics [64].

Clinical Applications

Volatile anesthetics are administered to provide amnesia and blunt the response to surgical stimulation, but can be of use in patients that have obstructive airway diseases or experience bronchoconstriction in the operating room. Multiple case reports provide examples of how volatile agents were used solely for the treatment of status asthmaticus [65–68].

Side Effects

The main concern with the use of volatile anesthetics is the rare occurrence of malignant hyperthermia. Hypotension can also be a concern with volatile anesthetics; however the blood pressure is usually easily restored with small amounts of IV fluids or vasopressors. Deep levels of anesthesia associated with high concentrations of volatile anesthetics may be undesirable, and prolonged administration outside the operating room is problematic.

Intravenous Anesthetics

Intravenous anesthetics can have positive effects on bronchomotor tone when used for induction or intravenous anesthesia in the operating room. Ketamine, propofol, and midazolam

(see Table 8.3) have relaxant effects on airway smooth muscle [69]. Etomidate and thiobarbiturates do not affect bronchomotor tone to the same extent [70]. The choice of intravenous anesthetics for induction and maintenance of anesthesia may be important for a patient with hard to manage bronchospasm or reactive airway disease.

Mechanism of Action

The precise mechanism of reduction of bronchomotor tone for the intravenous anesthetics is largely unknown. Ketamine is thought to have a direct relaxant effect on smooth muscle [71]. Propofol is thought to reduce vagal tone and have a direct effect on muscarinic receptors by interfering with cellular signaling and inhibiting calcium mobilization [72, 73]. The preservative metabisulfite in propofol prevents the inhibition of vagal-mediated bronchoconstriction [74].

Clinical Applications

Choosing an agent such as propofol or ketamine can be beneficial in patients with bronchospasm or obstructive airway disease [69, 70]. The use of these intravenous agents for induction or maintenance of anesthesia over other agents can be useful in minimizing the intraoperative effects of bronchospasm.

Side Effects

Although each of the intravenous anesthetics carries a unique side-effect profile, the major effects are not related to the airway. The use of ketamine is associated with increased salivation and coadministration of a small dose of anticholinergic can attenuate secretion production. Propofol is associated with hypotension that usually is easily corrected with IV fluids and vasopressors.

Local Anesthetics

Local anesthetics are primarily used to suppress coughing and blunt the hemodynamic response to tracheal intubation [75, 76]. Although animal models have demonstrated some ability of local anesthetics to relax bronchial smooth, in clinical practice the use of local anesthetics as pure bronchodilators is limited by toxicity and the ready availability of more potent bronchodilators such as short-acting beta-adrenergic agonists [71].

Influence of Adjunctive Agents on the Airway

Heliox

Helium (administered as a mixture of helium and oxygen [heliox]) has the advantage of having a low Reynolds' number and less resistance during turbulent airflow especially in large airways [6]. Helium and oxygen mixtures are recommended

as alternative therapies in asthma to support patients when traditional therapies have initially failed to make improvements [16, 58]. A recent trial in patients with COPD exacerbations failed to demonstrate a statistically significant reduction in the necessity for endotracheal intubation in patients treated with noninvasive ventilation and helium/oxygen mixtures [77]. The use of helium–oxygen mixtures is limited by a progressive reduction in efficacy at higher inspired oxygen concentrations.

Antihistamines

Histamine release from mast cells and basophils is responsible for airway inflammation and bronchoconstriction in asthma [78]. Antihistamines are not standard therapy for asthma, but the use of antihistamines and leukotriene modifiers for allergen-induced bronchoconstriction has shown promise for diminishing the early and late responses to allergens [78, 79]. Patients that have allergen-induced asthma or patients that experience an allergic reaction in the operating room may benefit from antihistamines to attenuate the role that histamine plays in bronchoconstriction.

Magnesium Sulfate

Magnesium sulfate is not a standard therapy for asthma exacerbations. Magnesium sulfate is thought to produce additional bronchodilation when given in conjunction with standard therapy for asthma exacerbations. Currently, intravenous magnesium therapy is reserved as an alternative therapy when the patient has not responded to standard therapy [16, 58, 80]. The combination of nebulized magnesium sulfate and beta-adrenergic agonists has also been studied and shows potential benefit in asthma exacerbations [81]. Overall, magnesium sulfate, IV or nebulized, is not a first-line therapy for asthma exacerbations and should be reserved for situations when the patient is not responding to conventional therapy [16, 58].

Summary

Patients with obstructive lung diseases presenting to the operating room for thoracic surgical procedures usually will be receiving pharmacotherapy to modify their symptoms or disease process. Understanding the role of pharmacotherapy in obstructive lung disease is essential to proper preoperative evaluation, perioperative risk reduction, and intraoperative management.

Clinical Case

A 65-year-old-man with COPD who quit smoking 2 years ago now presents to the preoperative clinic for evaluation before a right upper lobe lobectomy for a lung nodule. The patient has no other medical history and a recent cardiac stress test is normal.

Questions

Preoperative Evaluation:

- What medications for the treatment of COPD is the patient receiving?
- How often does he need rescue inhalers?
- When was the last time he was in the hospital with a COPD exacerbation?
- When was the last time he needed systemic corticosteroids for an exacerbation?
- Has there been any recent change in sputum or use of antibiotics?

Intraoperative Management:

- What medications will provide quickest relief of wheezing?
- Are prophylactic IV corticosteroids indicated?
- What role do helium/oxygen mixtures and magnesium sulfate play in the management of wheezing?

Answers

Preoperative Evaluation:

- This patient will likely present on an IC and long-acting beta-adrenergic agonist combination along with an anticholinergic such as ipratropium.
- Asking patients about the use of rescue inhalers gives some indication of how well their symptoms are controlled at baseline.
- Inquiring about previous hospitalizations and the extent of illness (i.e., intubation, ICU admission) is important in determining the severity of disease.
- The most recent use of systemic corticosteroids not only provides information as to how well the disease is being controlled, but also gives the evaluator an idea if the patient is prone to adrenal suppression during surgical stress.
- Discussing the use of antibiotics and changes in sputum allows the evaluator to know if the patient is experiencing an exacerbation or if the patient is at risk for infection with multidrug resistant bacteria.

Intraoperative Management:

- Intraoperative wheezing can be due to endotracheal intubation, light anesthesia, or allergic reaction. Starting with short-acting beta-2 adrenergic agonists, followed by inhaled anticholinergics, will give the most prompt relief. The additional use of intravenous and inhaled anesthetics may also be an effective treatment of bronchoconstriction.
- Prophylactic IV corticosteroids are not indicated. Steroids should be given if the patient has recently received steroids and stress doses are needed or the patient experiences an allergic reaction and steroids are administered to reduce the inflammatory response associated with the exposure.
- Helium/oxygen mixtures and magnesium sulfate are only indicated when the patient fails to adequately respond to maximum conventional therapy.

References

1. Jordan D. Central nervous pathways and control of the airways. *Respir Physiol*. 2001;125(1-2):67-81.
2. Lewis MJ, Short AL, Lewis KE. Autonomic nervous system control of the cardiovascular and respiratory systems in asthma. *Respir Med*. 2006;100(10):1688-705.
3. Burwell DR, Jones JG. The airways and anaesthesia – I. Anatomy, physiology and fluid mechanics. *Anaesthesia*. 1996;51(9):849-57.
4. Canning BJ, Fischer A. Neural regulation of airway smooth muscle tone. *Respir Physiol*. 2001;125(1-2):113-27.
5. Barnes Peter J. Pharmacology of airway smooth muscle. *Am J Respir Crit Care Med*. 1998;158(5):S123-32.
6. Lumb AB, Nunn JF. Nunn's applied respiratory physiology. 6th ed. Edinburgh: Elsevier Butterworth Heinemann; 2005.
7. Johnson M. The beta-adrenoceptor. *Am J Respir Crit Care Med*. 1998;158(5 Pt 3):S146-53.
8. Widdicombe JG. Autonomic regulation. i-NANC/e-NANC. *Am J Respir Crit Care Med*. 1998;158((5 Pt 3)):S171-5.
9. Drazen JM, Gaston B, Shore SA. Chemical regulation of pulmonary airway tone. *Annu Rev Physiol*. 1995;57:151-70.
10. Fanta CH. Asthma. *N Engl J Med*. 2009;360(10):1002-14.
11. Nelson HS. Beta-adrenergic bronchodilators. *N Engl J Med*. 1995;333(8):499-506.
12. Johnson M, Butchers PR, Coleman RA, et al. The pharmacology of salmeterol. *Life Sci*. 1993;52(26):2131-43.
13. Drazen JM, Israel E, Boushey HA, et al. Comparison of regularly scheduled with as-needed use of albuterol in mild asthma. *Asthma Clinical Research Network*. *N Engl J Med*. 1996;335(12):841-7.
14. Israel E, Chinchilli VM, Ford JG, et al. Use of regularly scheduled albuterol treatment in asthma: genotype-stratified, randomised, placebo-controlled cross-over trial. *Lancet*. 2004;364(9444):1505-12.
15. Israel E, Drazen JM, Liggett SB, et al. The effect of polymorphisms of the beta(2)-adrenergic receptor on the response to regular use of albuterol in asthma. *Am J Respir Crit Care Med*. 2000;162(1):75-80.
16. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma – Summary Report 2007. 2009. http://www.nhlbi.nih.gov/health/pubs/pub_prof.htm#asthma. Accessed 29 Dec 2009.
17. Gibson PG, Powell H, Ducharme FM. Differential effects of maintenance long-acting beta-agonist and inhaled corticosteroid on asthma control and asthma exacerbations. *J Allergy Clin Immunol*. 2007;119(2):344-50.
18. Bengtsson B. Plasma concentration and side-effects of terbutaline. *Eur J Respir Dis Suppl*. 1984;134:231-5.
19. Teule GJ, Majid PA. Haemodynamic effects of terbutaline in chronic obstructive airways disease. *Thorax*. 1980;35(7):536-42.
20. Wagner PD, Dantzker DR, Iacovoni VE, Tomlin WC, West JB. Ventilation-perfusion inequality in asymptomatic asthma. *Am Rev Respir Dis*. 1978;118(3):511-24.
21. Repsher LH, Anderson JA, Bush RK, et al. Assessment of tachyphylaxis following prolonged therapy of asthma with inhaled albuterol aerosol. *Chest*. 1984;85(1):34-8.
22. Georgopoulos D, Wong D, Anthonisen NR. Tolerance to beta 2-agonists in patients with chronic obstructive pulmonary disease. *Chest*. 1990;97(2):280-4.

23. Nelson HS, Weiss ST, Bleeker ER, Yancey SW, Dorinsky PM. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. *Chest*. 2006;129(1):15–26.
24. Williams SJ, Winner SJ, Clark TJ. Comparison of inhaled and intravenous terbutaline in acute severe asthma. *Thorax*. 1981;36(8):629–31.
25. Pierce RJ, Payne CR, Williams SJ, Denison DM, Clark TJ. Comparison of intravenous and inhaled terbutaline in the treatment of asthma. *Chest*. 1981;79(5):506–11.
26. Spiteri MA, Millar AB, Pavia D, Clarke SW. Subcutaneous adrenaline versus terbutaline in the treatment of acute severe asthma. *Thorax*. 1988;43(1):19–23.
27. Flynn RA, Glynn DA, Kennedy MP. Anticholinergic treatment in airways diseases. *Adv Ther*. 2009;26(10):908–19.
28. Karpel JP, Schacter EN, Fanta C, et al. A comparison of ipratropium and albuterol vs albuterol alone for the treatment of acute asthma. *Chest*. 1996;110(3):611–6.
29. Restrepo RD. A stepwise approach to management of stable COPD with inhaled pharmacotherapy: a review. *Respir Care*. 2009;54(8):1058–81.
30. Tashkin DP, Celli B, Senn S, et al. A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med*. 2008;359(15):1543–54.
31. Gal TJ, Suratt PM. Atropine and glycopyrrolate effects on lung mechanics in normal man. *Anesth Analg*. 1981;60(2):85–90.
32. Gal TJ, Suratt PM, Lu JY. Glycopyrrolate and atropine inhalation: comparative effects on normal airway function. *Am Rev Respir Dis*. 1984;129(5):871–3.
33. Villetti G, Bergamaschi M, Bassani F, et al. Pharmacological assessment of the duration of action of glycopyrrolate vs tiotropium and ipratropium in guinea-pig and human airways. *Br J Pharmacol*. 2006;148(3):291–8.
34. Haddad EB, Patel H, Keeling JE, Yacoub MH, Barnes PJ, Belvisi MG. Pharmacological characterization of the muscarinic receptor antagonist, glycopyrrolate, in human and guinea-pig airways. *Br J Pharmacol*. 1999;127(2):413–20.
35. Tzelepis G, Komanapalli S, Tyler D, Vega D, Fulambarker A. Comparison of nebulized glycopyrrolate and metaproterenol in chronic obstructive pulmonary disease. *Eur Respir J*. 1996;9(1):100–3.
36. Sutherland ER, Martin RJ. Airway inflammation in chronic obstructive pulmonary disease: comparisons with asthma. *J Allergy Clin Immunol*. 2003;112(5):819–27; quiz 828.
37. Fujimoto K, Kubo K, Yamamoto H, Yamaguchi S, Matsuzawa Y. Eosinophilic inflammation in the airway is related to glucocorticoid reversibility in patients with pulmonary emphysema. *Chest*. 1999;115(3):697–702.
38. Pizzichini E, Pizzichini MM, Gibson P, et al. Sputum eosinophilia predicts benefit from prednisone in smokers with chronic obstructive bronchitis. *Am J Respir Crit Care Med*. 1998;158 (5 Pt 1):1511–7.
39. Chanez P, Bourdin A, Vachier I, Godard P, Bousquet J, Vignola AM. Effects of inhaled corticosteroids on pathology in asthma and chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2004;1(3):184–90.
40. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med*. 2000;343(5):332–6.
41. Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA*. 1997;277(11):887–91.
42. Calverley PM, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med*. 2007;356(8):775–89.
43. Barnes PJ. Molecular mechanisms of corticosteroids in allergic diseases. *Allergy*. 2001;56(10):928–36.
44. Pujols L, Mullol J, Torrego A, Picado C. Glucocorticoid receptors in human airways. *Allergy*. 2004;59(10):1042–52.
45. Singh S, Amin AV, Loke YK. Long-term use of inhaled corticosteroids and the risk of pneumonia in chronic obstructive pulmonary disease: a meta-analysis. *Arch Intern Med*. 2009;169(3):219–29.
46. Niewoehner DE, Erbland ML, Deupree RH, et al. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1999;340(25):1941–7.
47. McEvoy CE, Niewoehner DE. Adverse effects of corticosteroid therapy for COPD. A critical review. *Chest*. 1997;111(3):732–43.
48. Usery JB, Self TH, Muthiah MP, Finch CK. Potential role of leukotriene modifiers in the treatment of chronic obstructive pulmonary disease. *Pharmacotherapy*. 2008;28(9):1183–7.
49. Drazen JM, Israel E, O’Byrne PM. Drug therapy: treatment of asthma with drugs modifying the leukotriene pathway. *N Engl J Med*. 1999;340(3):197–206.
50. Reiss TF, Chervinsky P, Dockhorn RJ, Shingo S, Seidenberg B, Edwards TB. Montelukast, a once-daily leukotriene receptor antagonist, in the treatment of chronic asthma: a multicenter, randomized, double-blind trial. *Montelukast Clinical Research Study Group*. *Arch Intern Med*. 1998;158(11):1213–20.
51. Israel E, Rubin P, Kemp JP, et al. The effect of inhibition of 5-lipoxygenase by zileuton in mild-to-moderate asthma. *Ann Intern Med*. 1993;119(11):1059–66.
52. Brabson JH, Clifford D, Kerwin E, et al. Efficacy and safety of low-dose fluticasone propionate compared with zafirlukast in patients with persistent asthma. *Am J Med*. 2002;113(1):15–21.
53. Malmstrom K, Rodriguez-Gomez G, Guerra J, et al. Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma. A randomized, controlled trial. *Montelukast/Beclomethasone Study Group*. *Ann Intern Med*. 1999;130(6):487–95.
54. Price DB, Hernandez D, Magyar P, et al. Randomised controlled trial of montelukast plus inhaled budesonide versus double dose inhaled budesonide in adult patients with asthma. *Thorax*. 2003;58(3):211–6.
55. Bernstein IL. Cromolyn sodium. *Chest*. 1985;87(1 Suppl):68S–73.
56. Guevara JP, Ducharme FM, Keren R, Nihtianova S, Zorc J. Inhaled corticosteroids versus sodium cromoglycate in children and adults with asthma. *Cochrane Database Syst Rev*. 2006;(2):CD003558.
57. Barnes PJ. Theophylline: new perspectives for an old drug. *Am J Respir Crit Care Med*. 2003;167(6):813–8.
58. Global Initiative for Asthma. <http://www.ginasthma.com>. 2009. Accessed 5 Jan 2010.
59. Global Initiative for Chronic Obstructive Lung Disease. <http://www.goldcopd.com>. 2009. Accessed 7 Jan 2010.

60. Aubier M, De Troyer A, Sampson M, Macklem PT, Roussos C. Aminophylline improves diaphragmatic contractility. *N Engl J Med.* 1981;305(5):249–52.
61. Goff MJ, Arain SR, Ficke DJ, Uhrich TD, Ebert TJ. Absence of bronchodilation during desflurane anesthesia: a comparison to sevoflurane and thiopental. *Anesthesiology.* 2000;93(2):404–8.
62. Rooke GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation. *Anesthesiology.* 1997;86(6):1294–9.
63. Yamakage M. Direct inhibitory mechanisms of halothane on canine tracheal smooth muscle contraction. *Anesthesiology.* 1992;77(3):546–53.
64. Yamakage M, Chen X, Tsujiguchi N, Kamada Y, Namiki A. Different inhibitory effects of volatile anesthetics on T- and L-type voltage-dependent Ca²⁺ channels in porcine tracheal and bronchial smooth muscles. *Anesthesiology.* 2001;94(4):683–93.
65. Gold MI, Helrich M. Pulmonary mechanics during general anesthesia: V. Status asthmaticus. *Anesthesiology.* 1970;32(5):422–8.
66. Parnass SM, Feld JM, Chamberlin WH, Segil LJ. Status asthmaticus treated with isoflurane and enflurane. *Anesth Analg.* 1987;66(2):193–5.
67. Johnston RG, Noseworthy TW, Friesen EG, Yule HA, Shustack A. Isoflurane therapy for status asthmaticus in children and adults. *Chest.* 1990;97(3):698–701.
68. Schwartz SH. Treatment of status asthmaticus with halothane. *JAMA.* 1984;251(20):2688–9.
69. Cheng EY, Mazzeo AJ, Bosnjak ZJ, Coon RL, Kampine JP. Direct relaxant effects of intravenous anesthetics on airway smooth muscle. *Anesth Analg.* 1996;83(1):162–8.
70. Eames WO, Rooke GA, Wu RS, Bishop MJ. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. *Anesthesiology.* 1996;84(6):1307–11.
71. Wanna HT, Gergis SD. Procaine, lidocaine, and ketamine inhibit histamine-induced contracture of guinea pig tracheal muscle in vitro. *Anesth Analg.* 1978;57(1):25–7.
72. Lin CC, Shyr MH, Tan PP, et al. Mechanisms underlying the inhibitory effect of propofol on the contraction of canine airway smooth muscle. *Anesthesiology.* 1999;91(3):750–9.
73. Brown RH, Wagner EM. Mechanisms of bronchoprotection by anesthetic induction agents: propofol versus ketamine. *Anesthesiology.* 1999;90(3):822–8.
74. Brown RH, Greenberg RS, Wagner EM. Efficacy of propofol to prevent bronchoconstriction: effects of preservative. *Anesthesiology.* 2001;94(5):851–5; discussion 856A.
75. Yukioka H, Hayashi M, Terai T, Fujimori M. Intravenous lidocaine as a suppressant of coughing during tracheal intubation in elderly patients. *Anesth Analg.* 1993;77(2):309–12.
76. Hamill JF, Bedford RF, Weaver DC, Colohan AR. Lidocaine before endotracheal intubation: intravenous or laryngotracheal? *Anesthesiology.* 1981;55(5):578–81.
77. Maggiore SM, Richard JC, Abroug F, et al. A multicenter, randomized trial of noninvasive ventilation with helium-oxygen mixture in exacerbations of chronic obstructive lung disease. *Crit Care Med.* 2010;38(1):145–51.
78. Lordan JL, Holgate ST. H1-antihistamines in asthma. *Clin Allergy Immunol.* 2002;17:221–48.
79. Richter K, Gronke L, Janicki S, Maus J, Jorres RA, Magnussen H. Effect of azelastine, montelukast, and their combination on allergen-induced bronchoconstriction in asthma. *Pulm Pharmacol Ther.* 2008;21(1):61–6.
80. Rowe BH, Bretzlaaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev.* 2000;(2):CD001490.
81. Blitz M, Blitz S, Hughes R, et al. Aerosolized magnesium sulfate for acute asthma: a systematic review. *Chest.* 2005;128(1):337–44.

Pharmacology of the Pulmonary Circulation

Cara Reimer and John Granton

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Abbreviations

CO	Cardiac output
(m)PAP	(Mean) pulmonary artery pressure
PHTN	Pulmonary hypertension
PVB	Paravertebral block
PVR(I)	Pulmonary vascular resistance (index)
SVR(I)	Systemic vascular resistance (index)
TEA	Thoracic epidural analgesia

Key Points

- The pulmonary vasculature is a complex system and studies of the effects of anesthetic drugs on this system are often contradictory.
- A balanced anesthetic technique with adherence to the hemodynamic goals of maintenance of right ventricular preload and right coronary perfusion is the safest choice for patients with PHTN.
- There are no absolute contraindications to most anesthetic drugs in patients with pulmonary hypertension.
- Inhaled pulmonary vasodilators can be used to optimize hemodynamic variables perioperatively, although effects on gas exchange are variable.

Introduction

Patients with pulmonary hypertension (PHTN) are high-risk candidates for noncardiac surgery. They have poor cardiorespiratory reserve and are at risk of having perioperative complications including pulmonary hypertensive crises with resultant heart failure, respiratory failure, and arrhythmias

[1, 2]. Anesthetic management of these patients can be complex and challenging. Drugs affecting the pulmonary vascular bed are routinely administered perioperatively in thoracic anesthesia, and their effects are of particular interest in patients with PHTN. Reducing the consequences of an elevated pulmonary vascular resistance and the resulting right ventricular dysfunction should be considered as the primary goal of therapy with vasodilators. Owing to the contractile properties of the naïve RV, attempts at improving its contractility are generally not effective. Therefore, principles of management of PHTN center on reducing RV afterload while preserving coronary perfusion by avoiding reductions in systemic blood pressure [3]. The effects of anesthetic drugs on the pulmonary vasculature bed and perioperative pulmonary vasodilator therapy are reviewed in this chapter, with special emphasis on perioperative drug choices in these patients.

Anesthetic Drugs

Evaluating the effects of anesthetic drugs on the pulmonary vasculature is challenging. In clinical practice and research, these drugs are rarely administered in isolation. Their administration can lead to concurrent changes in nonpulmonary hemodynamic parameters such as cardiac output (CO) that ultimately affect pulmonary artery pressure (PAP). An increase in PAP may be the result of increased PVR, increased CO, or an increase in LAP (PAP=(PVR×CO)+LAP). In addition, general anesthesia involves manipulation of variables that affect PVR, including FiO_2 , carbon dioxide (CO_2) and positive pressure ventilation (PPV). Issues that arise in interpreting studies and making useful conclusions include reliance on and extrapolation from animal data, small study sample sizes,

the questionable application of results in normal patients to patients with PHTN, children to adults and vice versa, and a vast supply of contradictory results. It is with acknowledgement of these limitations that we review the effects of routinely-administered anesthetic drugs on the pulmonary system.

Ketamine

Historically, ketamine has occupied a controversial position in anesthesia for patients with PHTN. Despite its current widespread use in these challenging patients, it has been classically taught that ketamine causes pulmonary vasoconstriction and should be used with extreme caution in this group.

The mechanism of action of ketamine is complex and not fully elucidated. It is an *N*-methyl-D-aspartic acid (NMDA) receptor antagonist, and also binds to opioid receptors and muscarinic receptors [4]. It appears to stimulate release [5] as well as inhibit neuronal uptake of catecholamines [6] which may account for its cardiotonic and bronchodilatory effects. Some animal studies have shown an endothelium-independent vasodilatory response to ketamine in the pulmonary bed [7, 8].

The effects of ketamine on the human pulmonary vasculature appear to be complex, and indeed, review of the clinical literature reveals a vast heterogeneity in regards to results. Factors known to affect pulmonary vasoreactivity such as FiO_2 , CO_2 , presence of PHTN, and presence of premedicants are not reported or acknowledged in many studies. The hemodynamic effects of a bolus of ketamine can be attenuated or abolished with premedicants like droperidol [9], dexmedetomidine [10] or benzodiazepines [11].

Early study of the drug's hemodynamic profile in adult patients showed increases of PAP and PVR in the range of 40–50% [12, 13]. This, combined with increases in variables contributing to myocardial oxygen consumption, raised concern about the use of ketamine in patients with CAD and PHTN. More recently in the pediatric literature, Williams et al. [14] showed no change in PVR or mean pulmonary artery pressure (mPAP) after ketamine administration in spontaneously breathing children with severe PHTN undergoing cardiac catheterization. In another pediatric study, ketamine maintained pulmonary to systemic blood flow and did not affect pulmonary pressure or resistance in children with intracardiac shunt undergoing cardiac catheterization. Propofol, on the other hand, decreased SVR leading to increased right to left shunting in this study [15]. As part of a balanced anesthetic induction for open lung biopsy, ketamine has been used in Eisenmenger syndrome with good results [16]. In adult patients undergoing OLV for lung resection, ketamine did not significantly increase PAP or PVR compared to enflurane [17]. Other case reports highlight the value of the relative cardiostability of the drug in patients with minimal cardiorespiratory reserve [18, 19]. At the time of this writing, the authors are unaware of any randomized studies addressing the use of

ketamine in adult patients with idiopathic pulmonary arterial hypertension (or other World Health Organization – WHO class 1 PAH subgroups) [20]. Many clinicians, including those at our institution, incorporate this drug into their routine inductions for patients with severe PHTN (pulmonary endarterectomy, lung transplantation). The advantages, in particular maintenance of stable hemodynamics and coronary perfusion pressure, seem to outweigh the potential disadvantages.

Propofol

Propofol is ubiquitously used in anesthesia, including for patients with PHTN. It is frequently used to maintain anesthesia during and after lung transplantation. The effects of propofol are thought to be primarily mediated by GABA receptors [21]. As mentioned in the discussion on ketamine, the concerning hemodynamic effect of propofol in the context of PHTN is a decrease in SVR, which can not only have effects on intracardiac shunting if present, but can also lead to decreased coronary artery perfusion of the right ventricle and resultant right ventricular dysfunction. In regards to direct effects on the pulmonary vasculature, animal studies have shown that during increased tone conditions in the pulmonary vasculature, propofol may act as a pulmonary vasoconstrictor [22, 23]. Propofol has also been shown to interfere with acetylcholine-induced pulmonary vasodilation in dogs [24]. On the other hand, in isolated pulmonary arteries from human and chronically hypoxic rats, etomidate and to a lesser-extent propofol showed vessel relaxation [25]. The clinical significance of these contradictory results is unknown.

Etomidate

Etomidate is an imidazole that mediates its clinical actions primarily at GABA A receptors. As mentioned above, it appears to have vasorelaxant properties in isolated pulmonary arteries [25]. Its major attribute as an induction agent is its stable hemodynamic profile. In patients with cardiac disease, an induction dose of etomidate increased MAP, decreased SVR, and decreased PAP [26]. In pediatric patients without PHTN presenting for cardiac catheterization, there was no significant change in any hemodynamic parameters after induction with etomidate [27].

Volatile Anesthetics

At clinically-relevant concentrations, modern volatile anesthetics likely have little to no direct vasodilating effect on the pulmonary vasculature. In a dog model (without PHTN), isoflurane decreased right ventricular function more than left ventricular function with no effect on PVR [28]. Likewise in pigs, sevoflurane administration depressed right ventricular function with no change in PVR [29]. This suggests that the decreases in PAP observed with volatile anesthetics [30] may partially occur secondary to the decreases in CO seen with

these agents. Nitrous oxide is typically avoided in patients with PHTN as it is believed to cause pulmonary vasoconstriction, perhaps via release of catecholamines from sympathetic nerves supplying the pulmonary vasculature [31]. In patients with mitral stenosis and PHTN presenting for cardiac surgery, administration of nitrous oxide after fentanyl anesthesia (7.5–10 µg/kg) increased PVR, PAP, and CI [32]. However, a subsequent study showed that in the presence of high-dose fentanyl (50–75 µg/kg) 70% nitrous oxide is actually associated with a decrease in PAP and CO in patients with secondary PHTN, with no echocardiographic changes in right ventricular function [33]. Interestingly, in univariate analysis in one retrospective cohort study, *not* using nitrous oxide was associated with postoperative mortality and increased length of stay in patients with PHTN presenting for noncardiac surgery [1]. There have been no studies to the authors' knowledge of the effects of nitrous oxide in patients with primary PHTN.

Opioids

Opioids seem to have little to no deleterious effects on the pulmonary vascular system. In anesthetized cats, administration of histamine, morphine, fentanyl, remifentanil and sufentanil caused a vasodilatory response under elevated tone conditions in isolated lobar artery [34]. The mechanism seems to involve histamine- and opioid-mediated receptor pathways. Clinical experience would echo the cardiostability of judicious narcotic administration in hemodynamically-fragile patients.

Neuromuscular Blockers

Pancuronium increases PAP in dogs with lung injury [35]. It is theorized to do so indirectly by increases in CO and directly by increasing PVR, possibly by its antagonist actions at muscarinic receptors in the pulmonary vasculature. Rocuronium, *cis*-atracurium, and vecuronium have little to no effect on most cardiac indices in patients undergoing CABG [36, 37]. A review on NMBs and cardiac surgery has been recently published [38].

Magnesium

Magnesium is a vasodilator in both the systemic and pulmonary circulations. The mechanism of action of magnesium's effects on vasodilation is likely through its effects on membrane channels involved in calcium flux and through its action in the synthesis of cyclic AMP [39]. It would appear to be an important cofactor for endothelial-dependent pulmonary vasodilation [40]. It has been used successfully to wean nitric oxide in PHTN [41]. Increasing doses of magnesium in piglets with acute embolic PHTN decreased mean PAP, increased CO, and decreased PVR [42]. Magnesium has been used to treat persistent PHTN of the newborn, but controversy surrounds its use here and a recent systematic review concluded that there is a lack of evidence to support its use in this population [23].

Regional Analgesia

Pain can increase PVR [43]. Perioperative thoracic epidural analgesia (TEA) and paravertebral block (PVB) are used routinely in thoracic surgery. TEA may decrease PAP through decreases in CO or via attenuation of the pulmonary sympathetic outflow [44]. In pigs, TEA depresses right ventricular function in acute PHTN [45]. Unilateral thoracic PVB with lidocaine has been shown to decrease myocardial contractility up to 30% and significantly decrease systemic pressure; an effect that may be attenuated by epinephrine [46]. In general, the potential benefits of regional anesthesia in thoracic surgery typically outweigh the risks of hypotension and right ventricular dysfunction. As with most anesthetic interventions in patients with PHTN, careful titration and monitoring is paramount. Indeed, case reports illustrate successful use of epidural analgesia in this patient population [47, 48].

Vasopressors and Inotropes

Vasopressors and inotropes are commonly required in thoracic anesthesia to counteract the effects of cardiodepressant and vasodilating drugs. Treatment of hypotension in these patients can be difficult to manage given the typical cautious fluid administration in this patient population.

The innervation and receptor content of the pulmonary vasculature is complex. Neurotransmitter receptors in this system include those from the adrenergic, cholinergic, and dopaminergic families as well as histamine, serotonin, adenosine, purines and peptides [49]. The pulmonary vasculature's response to sympathetic activation will generally result in an increase in PVR [50]. In human pulmonary artery, administration of acetylcholine induces pulmonary relaxation [51].

The response of the pulmonary system to exogenous vasoinpressor administration is dependent on the clinical situation. Consequently, results of studies are heterogeneous. In anesthetized dogs without PHTN, dopamine, epinephrine, norepinephrine and phenylephrine all increase PAP to varying degrees by varying mechanisms but with no drug there is a significant increase in PVR [52]. Dopamine does not increase PVR after lung transplantation in pigs [53]. In anesthetized patients with chronic secondary PHTN undergoing cardiac surgery, both norepinephrine and phenylephrine increase PAP and pulmonary vascular resistance index (PVRI) with minimal change in CI [54]. Within the clinically-relevant MAP target in this study, norepinephrine decreased the mPAP to MAP ratio, but phenylephrine did not, suggesting it may be a better choice in this patient cohort. In a dog model of acute PHTN, however, phenylephrine restored perfusion to the ischemic right ventricle and therefore increased CO [55]. This is a relevant observation, as it illustrates the importance of coronary artery perfusion in the setting of right ventricular strain and that maintenance of systemic pressure by whatever method may be the most important guiding principle in this subset of patients.

Vasopressin has also been studied. In a chronic hypoxic rat model, vasopressin administration resulted in a V1-receptor-mediated pulmonary vasodilation [56]. In an acute PHTN model in dogs, vasopressin increased PVR and resulted in a substantial decrease in right ventricular contractility [57]. Human studies of effects of vasopressin on the pulmonary vasculature are limited. Vasopressin has been used successfully after cardiac surgery in patients with PHTN and resistant hypotension [58]. The use of vasopressin to treat acute right ventricular failure in patients with IPPH has been described in obstetric anesthesia [59].

Pulmonary Vasodilators

Pulmonary vasodilators are typically employed to improve right ventricular function in the setting of PHTN or in an effort to enhance regional pulmonary blood flow and improve intrapulmonary shunt. In the acute care setting however, it is these agent's pulmonary vasodilatory effects that are being exploited. In general, parenteral and oral vasodilators are hampered by their relatively nonselective actions in the pulmonary vascular bed. In addition to their hypotensive systemic hemodynamic effects their use may also lead to perfusion of under-ventilated alveoli, worsen intrapulmonary shunt and, in turn, worsen oxygenation. The ideal pulmonary vasodilator should have a rapid onset of action, a short half-life, and produce regional pulmonary vasodilation. This would avoid systemic hypotension and the potential adverse effects on ventilation-perfusion matching that limit the utility of systemic agents in critically ill patients. In this regard inhaled vasodilators are attractive as they preferentially dilate ventilated alveoli and have less systemic effects.

Nitric Oxide

Inhaled nitric oxide (iNO) is preferentially delivered to ventilated lung units leading to improved perfusion to alveoli that are able to participate in gas exchange. This "selective effect" leads to a decrease in intrapulmonary shunt [60, 61]. Medical grade nitric oxide is made to be administered either noninvasively or through a ventilator circuit using a device that can regulate the concentration of NO and monitor levels of nitrogen dioxide – a byproduct of NO when it combines with oxygen. At present iNO is only approved for infants with respiratory distress syndrome. This approval stems from two large prospective placebo-controlled studies demonstrating that NO reduced the need for ECMO and reduced the requirement for oxygen therapy following ICU discharge [62, 63]. Although there is controversy about a dose-response relationship for NO and pulmonary vasodilation, the typical dose ranges from 10 to 40 ppm [64]. Methemoglobin levels need to be monitored when NO is administered for more than 24 h. Heart and lung transplantation represent two distinct areas where acute pulmonary vasodilation has strong theoretic benefit

as it relates to improving acute right ventricular failure and attenuating reperfusion injury, respectively. The acute right ventricular failure complicating heart transplantation may be attenuated with the use of a pulmonary vasodilator. Although several studies suggest that NO may be useful preoperatively in risk-stratifying patients scheduled for cardiac transplant, only case series support the use of inhaled NO to reverse the right ventricular dysfunction following cardiac transplant [65–69]. However, based on clinical experience, inhaled NO has become a standard of care in many transplant centers. The beneficial immune-modulating effects of inhaled NO in addition to its vasodilating properties were felt to be responsible for preliminary studies of using inhaled NO to prevent primary graft dysfunction (PGD) after lung transplantation [65, 70, 71]. Although a randomized clinical trial failed to show benefit in preventing PGD, it is commonly used to treat the hypoxemia and PHTN seen in established, severe PGD [72]. Owing to the inherent cost of using inhaled NO, other pulmonary vasodilators have been evaluated.

In nontransplant thoracic surgery, NO has been studied as a potential treatment for the gas exchange abnormalities associated with OLV. Its effects are controversial but it would appear that it exerts its maximal benefits in patients with elevated PVRI and the poorest gas exchange before administration [73–75]. There is no evidence for the routine use of this expensive drug in otherwise normal patients undergoing routine thoracic surgery.

Prostaglandins

Prostanoids induce relaxation of vascular smooth muscle, inhibit growth of smooth muscle cells, and are powerful inhibitors of platelet aggregation [76, 77]. Inhaled prostanoids involve an aerosol delivery mechanism that is attached by a nebulizer to the ventilator circuit. Treatment may be limited by inefficiencies in aerosolization. Owing to the short half-life of epoprostenol, the drug must also be continuously nebulized. As a result, changes of dose delivery with alterations in ventilator volumes, FiO_2 , airway pressures, and solvent evaporation may be challenging [3]. The synthetic prostanoids, treprostinil and iloprost, hold promise as inhaled vasodilators in that they may only require intermittent administration. Studies of these agents in chronic PAH demonstrated that they were effective in improving symptoms and exercise tolerance [78–81]. When nebulized, prostanoids can lead to similar improvements in oxygenation and pulmonary pressures as compared to inhaled NO [82–88]. A recent crossover study compared inhaled NO to inhaled prostaglandins in patients after lung ($n=19$) or heart ($n=6$) transplant. In this acute hemodynamic study, there was no significant difference in hemodynamics or oxygenation between agents [89].

Use of intravenous prostaglandins during OLV results in a decrease in both systemic and pulmonary pressures and either no change or a decrease in PaO_2 [90]. Selective infusion of prostaglandin into the pulmonary artery of the ventilated lung

in a dog model during OLV resulted in stable systemic pressure and a reduction in PVR and increase in PaO_2 [35]. However, this route of administration is not practical in routine thoracic anesthesia practice. Inhaled prostacyclin decreases PVRI and PAP with maintenance of favorable systemic pressures but does not change PaO_2 during OLV [91].

Both iNO and prostaglandins have been shown to affect platelet function [92, 93]. This could theoretically contribute to perioperative bleeding during large surgeries such as lung transplantation and is a concern in regards to neuraxial analgesia. The clinical relevance of platelet inhibition with these inhaled agents is unknown. Indeed, in cardiac surgery patients, laboratory confirmation of platelet dysfunction with inhaled prostacyclin did not correlate with chest tube losses [93]. Also, in an obstetrical patient with PHTN on intravenous prostacyclin, conversion to inhaled prostacyclin allowed for a successful labor epidural placement with no complications [94].

Phosphodiesterase Inhibitors

Phosphodiesterase inhibitors prevent the degradation of cyclic guanosine monophosphate (cGMP) and adenosine monophosphate (cAMP). Of relevance to this review, cAMP and cGMP are activated by nitric oxide (NO) and are intermediaries in a pathway that leads to vasodilation via the activation of protein kinases and reduction in cytosolic calcium.

Milrinone is an adenosine-3',5'-cyclic monophosphate (cAMP)-selective phosphodiesterase enzyme (PDE) inhibitor. When nebulized, it has been shown to lead to a relative reduction in PVR compared to SVR [95–97]. Haraldsson et al. evaluated a cohort of post-cardiac surgery patients and reported upon the hemodynamic effects of the combination inhaled milrinone and inhaled prostacyclins [98]. The inhalation of milrinone selectively dilated the pulmonary vasculature without systemic effects. When milrinone is combined with inhaled prostacyclin there appears to be a potentiation and prolongation of the pulmonary vasodilatory effect [98, 99].

Owing to the relatively higher expression of PDE5 in the pulmonary circulation relative to the systemic circulation, PDE5 inhibitors have a relative selective effect on PVR as opposed to SVR [100, 101]. In addition to their relatively selective pulmonary vasodilatory effects, their effects on smooth muscle proliferation and cellular apoptosis [102, 103] may be responsible for benefit of these agents when administered chronically in patients with idiopathic PAH [104, 105]. A direct effect on the right ventricle has been postulated, however, the clinical relevance of this finding is uncertain.

Although the benefits of sildenafil and tadalafil in chronic PAH have been evaluated in prospective controlled trials, most of the acute applications for these agents have been described in case reports or small cohort studies and as such have not been approved for these indications. In the acute setting, sildenafil has been demonstrated to enhance the

effects of inhaled NO and may also be useful in blunting the rebound in pulmonary pressures that occurs during weaning of inhaled NO [100, 106, 107]. The benefits of sildenafil in acute pulmonary embolism, cardiac transplantation and in patients with PHTN being considered for pulmonary thromboendarterectomy have also been described [108–112]. The merits of attempting to optimize RV function in patients with PHTN and planned pulmonary thromboendarterectomy were recently challenged in a retrospective analysis of chronic thromboembolic PHTN patients referred to a single center during 2005–2007. There was minimal benefit of treatment with medication on pre-PTE mPAP, but its use was associated with a significant delay in time to referral for PTE. Importantly, the two groups did not differ significantly in any post-PTE outcome. Although this study did not specifically evaluate the use of sildenafil for this purpose, it suggests at the very least, that planned, potentially curative surgery should not be delayed to explore theoretic benefits of this agent on RV function. Whether it can modify surgical risk in patients with very high PVR remains speculative. Although sildenafil has been advocated for use in patients with PHTN and left heart failure [113–115], and demonstrated a positive hemodynamic benefit in patients undergoing valve surgery [114], the negative results of a study evaluating continuous intravenous epoprostenol for the same purpose supports the notion that a controlled trial be conducted before these agents are routinely used for this purpose [116].

Conclusion

The aim of any anesthetic intervention in patients with PHTN is hemodynamic neutrality, which can be accomplished by a variety of agents and techniques. In general, no anesthetic drug is contraindicated in patients with PHTN. As with all anesthesia, an awareness of potential advantages and disadvantages of drugs is a key to proper decision-making. In the PHTN population, the general principles remain the same: adequate anesthesia and analgesia, maintenance of gas exchange to the best extent possible and support of the right ventricle. In reality, most clinicians who deal with these patients regularly use a wide variety of medications with success.

Although several studies have evaluated the acute hemodynamic responses to various pulmonary vasodilators, there are no randomized trials that have evaluated the effect of specific vasodilators on patient relevant outcomes. Methodological concerns of prior trials, uncertainties about efficacy, and concerns about safety (for both NO and prostaglandins) demand that proper prospective trials be undertaken.

Clinical Case Study

A 46-year-old woman with interstitial lung disease (ILD) presents to the Pre-Anesthetic Clinic before an open lung biopsy.

What are the Anesthetic Considerations for this Case?

Considerations include those if ILD and the proposed case itself. In regards to the ILD, its etiology and severity (including associated connective tissue disorders and multisystem involvement) and associated right heart dysfunction. In regards to the biopsy, the usual considerations of lung separation, analgesic options, invasive monitoring and, in this patient, the potential requirement for perioperative inhaled vasodilator therapy.

Besides the Usual Anesthetic History and Physical, What Would You Want to Elicit on History and Look for on Physical Exam in this Case?

On history, a careful assessment of functional status and current symptoms, personal and family history of connective tissue diseases.

On physical examination, respiratory rate, clubbing, crackles on lung auscultation, and signs of right heart dysfunction including increased JVP, hepatomegaly, lower extremity edema, increased P2 on heart auscultation and right ventricular heave on palpation.

The patient has been experiencing progressive worsening of shortness of breath for approximately 2 years. Her ability to exercise has declined markedly, to the point where she cannot climb a flight of stairs. She had a recent admission to hospital where she was started on home oxygen therapy and referred to a Respirologist. An echocardiogram done at that time revealed an RVSP of 89 with mild right ventricular dilation and hypokinesis. ECG shows sinus tachycardia at 105. The Respirologist suggests a biopsy to shed light on the etiology.

Physical examination reveals a thin woman with a respiratory rate of 18 wearing oxygen via nasal prongs at 4 L/min. Her oxygen saturation is 95%, her heart rate is 95, and her blood pressure is 100/60. Airway examination is reassuring. She has coarse crackles bilaterally. JVP is normal, but P2 is increased on cardiac auscultation. There is no hepatomegaly or pedal edema.

What Can Be Done to Optimize this Patients' Perioperative Course?

After communicating with the patient's Respirologist, a decision is made to bring the patient to the hospital the day before the planned operation to perform a right heart catheterization and assess the patient's response to inhaled prostacyclin. A pulmonary artery catheter is inserted under local anesthesia in the intensive care unit. PAP is 75/40. Systemic blood pressure is 90/60. After institution of inhaled prostacyclin, the PAP decreases to 60/30 with no change in systemic pressure.

What is the Anesthetic Plan?

TEE is arranged to be available for the case. After an appropriate fasting interval, the patient is transferred to the operating room with inhaled prostacyclin (10 ng/kg/min) and oxygen. A baseline ABG is drawn and shows: pH of 7.38, PaCO₂ 44, PaO₂ 65 and HCO₃ 28. Baseline vital signs are: heart rate 103, PAP 65/37, BP 98/62, 96% on FiO₂ 40%. An epidural is placed and tested at T5/6. An epidural infusion of bupivacaine and hydromorphone is started. Preoxygenation continues without interruption of the inhaled prostacyclin and norepinephrine is started at 0.05 µg/kg/min. After ensuring the surgeons are in the room, induction medications are titrated to effect and include midazolam 2 mg, fentanyl 250 µg and ketamine 50 mg. Rocuronium 50 mg is given to facilitate endotracheal intubation. A 37F left-sided double-lumen tube is placed without difficulty and anesthesia is maintained with sevoflurane and 100% oxygen. Inhaled prostacyclin is continued in the anesthetic circuit. Vital signs are stable with assumption of PPV. The patient is turned to the lateral position and surgery is started. After commencement of OLV, the patient's PAP climbs to 80/45, BP decreases to 78/40 and ST depression occurs in lead II on ECG. Oxygen saturation drops to 87% on 100%. Preexisting right ventricular hypokinesis and dilation are seen to worsen on TEE. A temporizing bolus of phenylephrine 200 µg is given while the norepinephrine is titrated up to 0.1 µg/kg/min. A bolus of 250 cc of normal saline is administered, keeping in mind the delicate balance between overloading a failing right ventricle and maintenance of adequate preload to ensure systemic CO. Inhaled prostacyclin is titrated up to 30 ng/kg/min. Vital signs move back toward baseline. The surgery is completed, the patient is extubated, awake and comfortable. Norepinephrine is titrated off in recovery and the prostacyclin is titrated down to baseline. The patient returns back to intensive care for close observation.

References

1. Ramakrishna G, Sprung J, Ravi BS, Chandrasekaran K, McGoon MD. Impact of pulmonary hypertension on the outcomes of non-cardiac surgery: predictors of perioperative morbidity and mortality. *J Am Coll Cardiol.* 2005;45(10):1691–9.
2. Lai HC, Wang KY, Lee WL, Ting CT, Liu TJ. Severe pulmonary hypertension complicates postoperative outcome of non-cardiac surgery. *Br J Anaesth.* 2007;99(2):184–90.
3. Granton J, Moric J. Pulmonary vasodilators – treating the right ventricle. *Anesthesiol Clin.* 2008;26(2):337–53. vii.
4. Hirota K, Lambert DG. Ketamine: its mechanism(s) of action and unusual clinical uses. *Br J Anaesth.* 1996;77(4):441–4.
5. Baraka A, Harrison T, Kachachi T. Catecholamine levels after ketamine anesthesia in man. *Anesth Analg.* 1973;52(2):198–200.
6. Lundy PM, Lockwood PA, Thompson G, Frew R. Differential effects of ketamine isomers on neuronal and extraneuronal catecholamine uptake mechanisms. *Anesthesiology.* 1986;64(3):359–63.

7. Maruyama K, Maruyama J, Yokochi A, Muneyuki M, Miyasaka K. Vasodilatory effects of ketamine on pulmonary arteries in rats with chronic hypoxic pulmonary hypertension. *Anesth Analg*. 1995;80(4):786–92.
8. Lee TS, Hou X. Vasoactive effects of ketamine on isolated rabbit pulmonary arteries. *Chest*. 1995;107(4):1152–5.
9. Balfors E, Haggmark S, Nyhman H, Rydwall A, Reiz S. Droperidol inhibits the effects of intravenous ketamine on central hemodynamics and myocardial oxygen consumption in patients with generalized atherosclerotic disease. *Anesth Analg*. 1983;62(2):193–7.
10. Levanen J, Makela ML, Scheinin H. Dexmedetomidine premedication attenuates ketamine-induced cardiostimulatory effects and postanesthetic delirium. *Anesthesiology*. 1995;82(5):1117–25.
11. Reich DL, Silvay G. Ketamine: an update on the first twenty-five years of clinical experience. *Can J Anaesth*. 1989;36(2):186–97.
12. Tweed WA, Minuck M, Mymin D. Circulatory responses to ketamine anesthesia. *Anesthesiology*. 1972;37(6):613–9.
13. Gooding JM, Dimick AR, Tavakoli M, Corssen G. A physiologic analysis of cardiopulmonary responses to ketamine anesthesia in noncardiac patients. *Anesth Analg*. 1977;56(6):813–6.
14. Williams GD, Philip BM, Chu LF, et al. Ketamine does not increase pulmonary vascular resistance in children with pulmonary hypertension undergoing sevoflurane anesthesia and spontaneous ventilation. *Anesth Analg*. 2007;105(6):1578–84.
15. Oklu E, Bulutcu FS, Yalcin Y, Ozbek U, Cakali E, Bayindir O. Which anesthetic agent alters the hemodynamic status during pediatric catheterization? Comparison of propofol versus ketamine. *J Cardiothorac Vasc Anesth*. 2003;17(6):686–90.
16. Heller AR, Litz RJ, Koch T. A fine balance – one-lung ventilation in a patient with Eisenmenger syndrome. *Br J Anaesth*. 2004;92(4):587–90.
17. Rees DI, Gaines III GY. One-lung anesthesia – a comparison of pulmonary gas exchange during anesthesia with ketamine or enflurane. *Anesth Analg*. 1984;63(5):521–5.
18. Aye T, Milne B. Ketamine anesthesia for pericardial window in a patient with pericardial tamponade and severe COPD. *Can J Anaesth*. 2002;49(3):283–6.
19. Kopka A, McMenemin IM, Serpell MG, Quasim I. Anaesthesia for cholecystectomy in two non-parturients with Eisenmenger's syndrome. *Acta Anaesthesiol Scand*. 2004;48(6):782–6.
20. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573–619.
21. Trapani G, Altomare C, Liso G, Sanna E, Biggio G. Propofol in anesthesia. Mechanism of action, structure-activity relationships, and drug delivery. *Curr Med Chem*. 2000;7(2):249–71.
22. Kondo U, Kim SO, Nakayama M, Murray PA. Pulmonary vascular effects of propofol at baseline, during elevated vasomotor tone, and in response to sympathetic alpha- and beta-adrenoreceptor activation. *Anesthesiology*. 2001;94(5):815–23.
23. Edanaga M, Nakayama M, Kanaya N, Tohse N, Namiki A. Propofol increases pulmonary vascular resistance during alpha-adrenoreceptor activation in normal and monocrotaline-induced pulmonary hypertensive rats. *Anesth Analg*. 2007;104(1):112–8.
24. Kondo U, Kim SO, Murray PA. Propofol selectively attenuates endothelium-dependent pulmonary vasodilation in chronically instrumented dogs. *Anesthesiology*. 2000;93(2):437–46.
25. Ouedraogo N, Mounkaila B, Crevel H, Marthan R, Roux E. Effect of propofol and etomidate on normoxic and chronically hypoxic pulmonary artery. *BMC Anesthesiol*. 2006;6:2.
26. Colvin MP, Savege TM, Newland PE, et al. Cardiorespiratory changes following induction of anaesthesia with etomidate in patients with cardiac disease. *Br J Anaesth*. 1979;51(6):551–6.
27. Sarkar M, Laussen PC, Zurkowski D, Shukla A, Kussman B, Odegard KC. Hemodynamic responses to etomidate on induction of anesthesia in pediatric patients. *Anesth Analg*. 2005;101(3):645–50.
28. Priebe HJ. Differential effects of isoflurane on regional right and left ventricular performances, and on coronary, systemic, and pulmonary hemodynamics in the dog. *Anesthesiology*. 1987;66(3):262–72.
29. Kerbaul F, Bellezza M, Mekkaoui C, et al. Sevoflurane alters right ventricular performance but not pulmonary vascular resistance in acutely instrumented anesthetized pigs. *J Cardiothorac Vasc Anesth*. 2006;20(2):209–16.
30. Cheng DC, Edelist G. Isoflurane and primary pulmonary hypertension. *Anaesthesia*. 1988;43(1):22–4.
31. Rorie DK, Tyce GM, Sill JC. Increased norepinephrine release from dog pulmonary artery caused by nitrous oxide. *Anesth Analg*. 1986;65(6):560–4.
32. Schulte-Sasse U, Hess W, Tarnow J. Pulmonary vascular responses to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology*. 1982;57(1):9–13.
33. Konstadt SN, Reich DL, Thys DM. Nitrous oxide does not exacerbate pulmonary hypertension or ventricular dysfunction in patients with mitral valvular disease. *Can J Anaesth*. 1990;37(6):613–7.
34. Kaye AD, Hoover JM, Kaye AJ, et al. Morphine, opioids, and the feline pulmonary vascular bed. *Acta Anaesthesiol Scand*. 2008;52(7):931–7.
35. Chen TL, Ueng TH, Huang CH, Chen CL, Huang FY, Lin CJ. Improvement of arterial oxygenation by selective infusion of prostaglandin E1 to ventilated lung during one-lung ventilation. *Acta Anaesthesiol Scand*. 1996;40(1):7–13.
36. McCoy EP, Maddineni VR, Elliott P, Mirakhur RK, Carson IW, Cooper RA. Haemodynamic effects of rocuronium during fentanyl anaesthesia: comparison with vecuronium. *Can J Anaesth*. 1993;40(8):703–8.
37. Searle NR, Thomson I, Dupont C, et al. A two-center study evaluating the hemodynamic and pharmacodynamic effects of cisatracurium and vecuronium in patients undergoing coronary artery bypass surgery. *J Cardiothorac Vasc Anesth*. 1999;13(1):20–5.
38. Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80–90.
39. Dube L, Granry JC. The therapeutic use of magnesium in anaesthesiology, intensive care and emergency medicine: a review. *Can J Anaesth*. 2003;50(7):732–46.
40. Fullerton DA, Hahn AR, Agrafojo J, Sheridan BC, McIntyre Jr RC. Magnesium is essential in mechanisms of pulmonary vasoconstrictor control. *J Surg Res*. 1996;63(1):93–7.
41. al-Halees Z, Afrane B, el-Barbary M. Magnesium sulfate to facilitate weaning of nitric oxide in pulmonary hypertension. *Ann Thorac Surg*. 1997;63(1):298–9.

42. Haas NA, Kemke J, Schulze-Neick I, Lange PE. Effect of increasing doses of magnesium in experimental pulmonary hypertension after acute pulmonary embolism. *Intensive Care Med.* 2004;30(11):2102–9.
43. Houfflin Debarge V, Sicot B, Jaillard S, et al. The mechanisms of pain-induced pulmonary vasoconstriction: an experimental study in fetal lambs. *Anesth Analg.* 2007;104(4):799–806.
44. Veering BT, Cousins MJ. Cardiovascular and pulmonary effects of epidural anaesthesia. *Anaesth Intensive Care.* 2000;28(6):620–35.
45. Rex S, Missant C, Segers P, Wouters PF. Thoracic epidural anaesthesia impairs the hemodynamic response to acute pulmonary hypertension by deteriorating right ventricular-pulmonary arterial coupling. *Crit Care Med.* 2007;35(1):222–9.
46. Garutti I, Olmedilla L, Cruz P, Pineiro P, De la Gala F, Cirujano A. Comparison of the hemodynamic effects of a single 5 mg/kg dose of lidocaine with or without epinephrine for thoracic paravertebral block. *Reg Anesth Pain Med.* 2008;33(1):57–63.
47. Armstrong P. Thoracic epidural anaesthesia and primary pulmonary hypertension. *Anaesthesia.* 1992;47(6):496–9.
48. Mallampati SR. Low thoracic epidural anaesthesia for elective cholecystectomy in a patient with congenital heart disease and pulmonary hypertension. *Can Anaesth Soc J.* 1983;30(1):72–6.
49. Kobayashi Y, Amenta F. Neurotransmitter receptors in the pulmonary circulation with particular emphasis on pulmonary endothelium. *J Auton Pharmacol.* 1994;14(2):137–64.
50. Barnes PJ, Liu SF. Regulation of pulmonary vascular tone. *Pharmacol Rev.* 1995;47(1):87–131.
51. Greenberg B, Rhoden K, Barnes PJ. Endothelium-dependent relaxation of human pulmonary arteries. *Am J Physiol.* 1987;252(2 Pt 2):H434–8.
52. Pearl RG, Maze M, Rosenthal MH. Pulmonary and systemic hemodynamic effects of central venous and left atrial sympathomimetic drug administration in the dog. *J Cardiothorac Anesth.* 1987;1(1):29–35.
53. Roscher R, Ingemansson R, Algotsson L, Sjoberg T, Steen S. Effects of dopamine in lung-transplanted pigs at 32 degrees C. *Acta Anaesthesiol Scand.* 1999;43(7):715–21.
54. Kwak YL, Lee CS, Park YH, Hong YW. The effect of phenylephrine and norepinephrine in patients with chronic pulmonary hypertension. *Anaesthesia.* 2002;57(1):9–14.
55. Vlahakes GJ, Turley K, Hoffman JI. The pathophysiology of failure in acute right ventricular hypertension: hemodynamic and biochemical correlations. *Circulation.* 1981;63(1):87–95.
56. Jin HK, Yang RH, Chen YF, Thornton RM, Jackson RM, Oparil S. Hemodynamic effects of arginine vasopressin in rats adapted to chronic hypoxia. *J Appl Physiol.* 1989;66(1):151–60.
57. Leather HA, Segers P, Berends N, Vandermeersch E, Wouters PF. Effects of vasopressin on right ventricular function in an experimental model of acute pulmonary hypertension. *Crit Care Med.* 2002;30(11):2548–52.
58. Tayama E, Ueda T, Shojima T, et al. Arginine vasopressin is an ideal drug after cardiac surgery for the management of low systemic vascular resistant hypotension concomitant with pulmonary hypertension. *Interact Cardiovasc Thorac Surg.* 2007;6(6):715–9.
59. Price LC, Forrest P, Sodhi V, et al. Use of vasopressin after Caesarean section in idiopathic pulmonary arterial hypertension. *Br J Anaesth.* 2007;99(4):552–5.
60. Michael JR, Barton RG, Saffle JR, et al. Inhaled nitric oxide versus conventional therapy: effect on oxygenation in ARDS [see comments]. *Am J Respir Crit Care Med.* 1998;157(5 Pt 1):1372–80.
61. Troncy E, Collet JP, Shapiro S, et al. Inhaled nitric oxide in acute respiratory distress syndrome: a pilot randomized controlled study. *Am J Respir Crit Care Med.* 1998;157(5 Pt 1):1483–8.
62. The Neonatal Inhaled Nitric Oxide Study Group (NINOS). Inhaled nitric oxide and hypoxic respiratory failure in infants with congenital diaphragmatic hernia. *Pediatrics.* 1997;99(6):838–45.
63. Roberts Jr JD, Fineman JR, Morin III FC, et al. Inhaled nitric oxide and persistent pulmonary hypertension of the newborn. The Inhaled Nitric Oxide Study Group. *N Engl J Med.* 1997;336(9):605–10.
64. Solina AR, Ginsberg SH, Papp D, et al. Dose response to nitric oxide in adult cardiac surgery patients. *J Clin Anesth.* 2001;13(4):281–6.
65. Meyer KC, Love RB, Zimmerman JJ. The therapeutic potential of nitric oxide in lung transplantation. *Chest.* 1998;113(5):1360–71.
66. Paniagua MJ, Crespo-Leiro MG, Rodriguez JA, et al. Usefulness of nitric oxide inhalation for management of right ventricular failure after heart transplantation in patients with pretransplant pulmonary hypertension. *Transplant Proc.* 1999;31(6):2505–6.
67. Ardehali A, Hughes K, Sadeghi A, et al. Inhaled nitric oxide for pulmonary hypertension after heart transplantation. *Transplantation.* 2001;72(4):638–41.
68. Mosquera I, Crespo-Leiro MG, Tabuyo T, et al. Pulmonary hypertension and right ventricular failure after heart transplantation: usefulness of nitric oxide. *Transplant Proc.* 2002;34(1):166–7.
69. Mahajan A, Shabanie A, Varshney SM, Marijic J, Sopher MJ. Inhaled nitric oxide in the preoperative evaluation of pulmonary hypertension in heart transplant candidates. *J Cardiothorac Vasc Anesth.* 2007;21(1):51–6.
70. Date H, Triantafillou AN, Trulock EP, Pohl MS, Cooper JD, Patterson GA. Inhaled nitric oxide reduces human lung allograft dysfunction. *J Thorac Cardiovasc Surg.* 1996;111(5):913–9.
71. Yamashita H, Akamine S, Sumida Y, et al. Inhaled nitric oxide attenuates apoptosis in ischemia-reperfusion injury of the rabbit lung. *Ann Thorac Surg.* 2004;78(1):292–7.
72. Meade MO, Granton JT, Matte-Martyn A, et al. A randomized trial of inhaled nitric oxide to prevent ischemia-reperfusion injury after lung transplantation. *Am J Respir Crit Care Med.* 2003;167(11):1483–9.
73. Wilson WC, Kapelanski DP, Benumof JL, Newhart II JW, Johnson FW, Channick RN. Inhaled nitric oxide (40 ppm) during one-lung ventilation, in the lateral decubitus position, does not decrease pulmonary vascular resistance or improve oxygenation in normal patients. *J Cardiothorac Vasc Anesth.* 1997;11(2):172–6.
74. Ismail-Zade IA, Vuylsteke A, Ghosh S, Latimer RD. Inhaled nitric oxide and one-lung ventilation in the lateral decubitus position. *J Cardiothorac Vasc Anesth.* 1997;11(7):926–7.
75. Rocca GD, Coccia C, Pompei L, et al. Hemodynamic and oxygenation changes of combined therapy with inhaled nitric oxide and inhaled aerosolized prostacyclin. *J Cardiothorac Vasc Anesth.* 2001;15(2):224–7.
76. Moncada S, Higgs EA. Prostaglandins in the pathogenesis and prevention of vascular disease. *Blood Rev.* 1987;1(2):141–5.
77. Vane JR, Botting RM. Pharmacodynamic profile of prostacyclin. *Am J Cardiol.* 1995;75(3):3A–10.
78. McLaughlin VV, Gaine SP, Barst RJ, et al. Efficacy and safety of treprostinil: an epoprostenol analog for primary pulmonary hypertension. *J Cardiovasc Pharmacol.* 2003;41(2):293–9.

79. Voswinckel R, Reichenberger F, Enke B, et al. Acute effects of the combination of sildenafil and inhaled treprostinil on haemodynamics and gas exchange in pulmonary hypertension. *Pulm Pharmacol Ther.* 2008;21(5):824–32.
80. Hoeper MM, Schwarze M, Ehlerding S, et al. Long-term treatment of primary pulmonary hypertension with aerosolized iloprost a prostacyclin analogue. *N Engl J Med.* 2000;342(25):1866–70.
81. Olschewski H, Simonneau G, Galie N, et al. Inhaled iloprost for severe pulmonary hypertension. *N Engl J Med.* 2002;347(5):322–9.
82. Fiser SM, Cope JT, Kron IL, et al. Aerosolized prostacyclin (epoprostenol) as an alternative to inhaled nitric oxide for patients with reperfusion injury after lung transplantation. *J Thorac Cardiovasc Surg.* 2001;121(5):981–2.
83. Langer F, Wendler O, Wilhelm W, Tscholl D, Schafers HJ. Treatment of a case of acute right heart failure by inhalation of iloprost, a long-acting prostacyclin analogue. *Eur J Anaesthesiol.* 2001;18(11):770–3.
84. Langer F, Wilhelm W, Lausberg H, Schafers HJ. Iloprost and selective pulmonary vasodilation. Clinical results of intraoperative and postoperative inhalation of iloprost. *Anaesthetist.* 2004;53(8):753–8.
85. Sablotzki A, Hentschel T, Gruenig E, et al. Hemodynamic effects of inhaled aerosolized iloprost and inhaled nitric oxide in heart transplant candidates with elevated pulmonary vascular resistance. *Eur J Cardiothorac Surg.* 2002;22(5):746–52.
86. Wensel R, Opitz C, Ewert R, Bruch L, Kleber F. Effects of iloprost inhalation on exercise capacity and ventilatory efficiency in patients with primary pulmonary hypertension. *Circulation.* 2000;101(20):2388–92.
87. Wittwer T, Franke UF, Fehrenbach A, et al. Donor pretreatment using the aerosolized prostacyclin analogue iloprost optimizes post-ischemic function of non-heart beating donor lungs. *J Heart Lung Transplant.* 2005;24(4):371–8.
88. Rex S, Schaelte G, Metzelder S, et al. Inhaled iloprost to control pulmonary artery hypertension in patients undergoing mitral valve surgery: a prospective, randomized-controlled trial. *Acta Anaesthesiol Scand.* 2008;52(1):65–72.
89. Khan TA, Schnickel G, Ross D, et al. A prospective, randomized, crossover pilot study of inhaled nitric oxide versus inhaled prostacyclin in heart transplant and lung transplant recipients. *J Thorac Cardiovasc Surg.* 2009;138(6):1417–24.
90. Bund M, Henzler D, Walz R, Rossaint R, Piepenbrock S. Cardiopulmonary effects of intravenous prostaglandin E1 during experimental one-lung ventilation. *Thorac Cardiovasc Surg.* 2006;54(5):341–7.
91. Bund M, Henzler D, Walz R, Rossaint R, Piepenbrock S, Kuhlen R. Aerosolized and intravenous prostacyclin during one-lung ventilation. Hemodynamic and pulmonary effects. *Anaesthetist.* 2004;53(7):612–20.
92. Nielsen VG. Nitric oxide decreases coagulation protein function in rabbits as assessed by thromboelastography. *Anesth Analg.* 2001;92(2):320–3.
93. Haraldsson A, Kieler-Jensen N, Wadenvik H, Ricksten SE. Inhaled prostacyclin and platelet function after cardiac surgery and cardiopulmonary bypass. *Intensive Care Med.* 2000;26(2):188–94.
94. Hill LL, De Wet CJ, Jacobsohn E, Leighton BL, Tymkew H. Peripartum substitution of inhaled for intravenous prostacyclin in a patient with primary pulmonary hypertension. *Anesthesiology.* 2004;100(6):1603–5.
95. Buckley MS, Feldman JP. Nebulized milrinone use in a pulmonary hypertensive crisis. *Pharmacotherapy.* 2007;27(12):1763–6.
96. Lamarche Y, Perrault LP, Maltais S, Tetreault K, Lambert J, Denault AY. Preliminary experience with inhaled milrinone in cardiac surgery. *Eur J Cardiothorac Surg.* 2007;31(6):1081–7.
97. Urdaneta F, Lobato EB, Beaver T, et al. Treating pulmonary hypertension post cardiopulmonary bypass in pigs: milrinone vs. sildenafil analog. *Perfusion.* 2008;23(2):117–25.
98. Haraldsson SA, Kieler-Jensen N, Ricksten SE. The additive pulmonary vasodilatory effects of inhaled prostacyclin and inhaled milrinone in postcardiac surgical patients with pulmonary hypertension. *Anesth Analg.* 2001;93(6):1439–45.
99. Lakshminrusimha S, Porta NF, Farrow KN, et al. Milrinone enhances relaxation to prostacyclin and iloprost in pulmonary arteries isolated from lambs with persistent pulmonary hypertension of the newborn. *Pediatr Crit Care Med.* 2009;10(1):106–12.
100. Ghofrani HA, Voswinckel R, Reichenberger F, et al. Differences in hemodynamic and oxygenation responses to three different phosphodiesterase-5 inhibitors in patients with pulmonary arterial hypertension: a randomized prospective study. *J Am Coll Cardiol.* 2004;44(7):1488–96.
101. Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S. Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension: comparison with inhaled nitric oxide. *Circulation.* 2002;105(20):2398–403.
102. Wharton J, Strange JW, Moller GM, et al. Antiproliferative effects of phosphodiesterase type 5 inhibition in human pulmonary artery cells. *Am J Respir Crit Care Med.* 2005;172(1):105–13.
103. Archer SL, Michelakis ED. Phosphodiesterase type 5 inhibitors for pulmonary arterial hypertension. *N Engl J Med.* 2009;361(19):1864–71.
104. Galie N, Brundage BH, Ghofrani HA, et al. Tadalafil therapy for pulmonary arterial hypertension. *Circulation.* 2009;119(22):2894–903.
105. Galie N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. *N Engl J Med.* 2005;353(20):2148–57.
106. Atz AM, Wessel DL. Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. *Anesthesiology.* 1999;91(1):307–10.
107. Bigatello LM, Hess D, Dennehy KC, Medoff BD, Hurford WE. Sildenafil can increase the response to inhaled nitric oxide. *Anesthesiology.* 2000;92(6):1827–9.
108. Suntharalingam J, Treacy CM, Doughty NJ, et al. Long-term use of sildenafil in inoperable chronic thromboembolic pulmonary hypertension. *Chest.* 2008;134(2):229–36.
109. Boffini M, Sansone F, Ceresa F, et al. Role of oral sildenafil in the treatment of right ventricular dysfunction after heart transplantation. *Transplant Proc.* 2009;41(4):1353–6.
110. De Santo LS, Mastrianni C, Romano G, et al. Role of sildenafil in acute posttransplant right ventricular dysfunction: successful experience in 13 consecutive patients. *Transplant Proc.* 2008;40(6):2015–8.

111. Ghofrani HA, Schermuly RT, Rose F, et al. Sildenafil for long-term treatment of nonoperable chronic thromboembolic pulmonary hypertension. *Am J Respir Crit Care Med.* 2003;167(8):1139–41.
112. Dias-Junior CA, Vieira TF, Moreno Jr H, Evora PR, Tanus-Santos JE. Sildenafil selectively inhibits acute pulmonary embolism-induced pulmonary hypertension. *Pulm Pharmacol Ther.* 2005;18(3):181–6.
113. Lewis GD, Shah R, Shahzad K, et al. Sildenafil improves exercise capacity and quality of life in patients with systolic heart failure and secondary pulmonary hypertension. *Circulation.* 2007;116(14):1555–62.
114. Shim JK, Choi YS, Oh YJ, Kim DH, Hong YW, Kwak YL. Effect of oral sildenafil citrate on intraoperative hemodynamics in patients with pulmonary hypertension undergoing valvular heart surgery. *J Thorac Cardiovasc Surg.* 2006;132(6):1420–5.
115. Zakliczynski M, Maruszewski M, Pyka L, et al. Effectiveness and safety of treatment with sildenafil for secondary pulmonary hypertension in heart transplant candidates. *Transplant Proc.* 2007;39(9):2856–8.
116. Califf RM, Adams KF, McKenna WJ, et al. A randomized controlled trial of epoprostenol therapy for severe congestive heart failure: The Flolan International Randomized Survival Trial (FIRST). *Am Heart J.* 1997;134(1):44–54.

10

Perioperative Lung Injury

Peter Slinger

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Key Points

- Traditional patterns of mechanical ventilation with large (e.g., 10–12 mL/kg) tidal volumes and without PEEP cause a subclinical injury in healthy lungs in proportion to the duration of ventilation.
- Perioperative acute lung injury becomes clinically important when injurious ventilation patterns are used in patients who have other concomitant lung injuries such as large pulmonary resection, cardiopulmonary bypass, or transfusion-related lung injury.
- Lung-protective patterns of mechanical ventilation, using more physiologic tidal volumes and appropriate PEEP, reduce the severity of this lung injury.
- A recent decrease in the incidence of lung injury after pulmonary resection is primarily due to a decrease in the frequency of pneumonectomies.

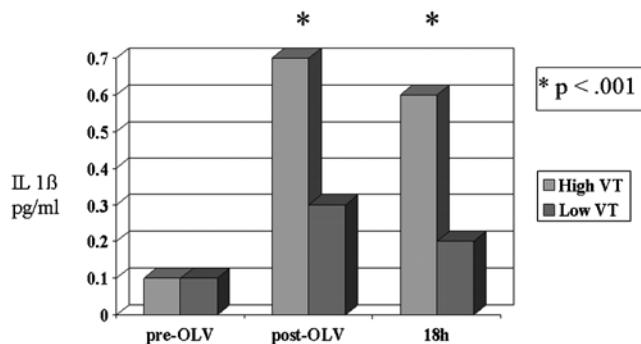
Introduction

Perioperative lung injury is defined as pneumonitis, acute lung injury (ALI), or acute respiratory distress syndrome (ARDS) occurring in the immediate postoperative period during the initial hospitalization. ALI and ARDS definitions include a $\text{PaO}_2/\text{FiO}_2$ ratio (ALI < 300 , ARDS < 200) and radiographic infiltrates characteristic of pulmonary edema in accordance with the American-European Consensus Conference Guidelines [1]. Lung injury following thoracic surgery has been described by a number of terms over the past 30 years including postpneumonectomy pulmonary

edema, permeability pulmonary edema, and postoperative lung injury. While other causes of postoperative morbidity and mortality in thoracic surgery such as atelectasis, pneumonia and bronchopleural fistula have declined dramatically in the past 30 years [2], lung injury remains a major problem and now has become the leading cause of death after pulmonary surgery [3].

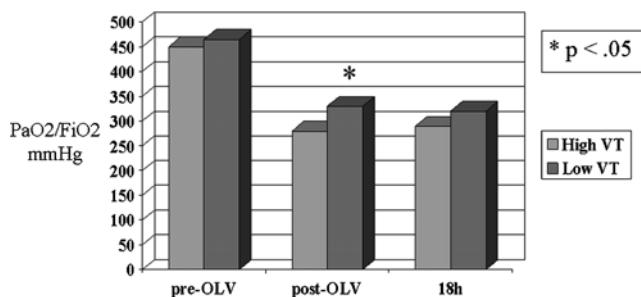
Acute Lung Injury in Patients with Healthy Lungs

Traditionally, anesthesiologists have been taught to ventilate patients in the operative and postoperative periods with relatively large tidal volumes. Volumes as large as 15 mL/kg ideal body weight have been suggested to avoid intraoperative atelectasis [4]. This far exceeds the normal spontaneous tidal volumes (5–6 mL/kg) common to most mammals [5]. It has become obvious that these nonphysiologic large tidal volumes can cause a degree of subclinical injury in healthy lungs. Gajic et al. [6] reported that 25% of patients without lung injury ventilated in an ICU setting for 2 days or longer developed ALI or ARDS. The main risk factors associated with the development of lung injury were the use of large tidal volumes, restrictive lung disease, and transfusion of blood products. In a prospective study, the same group found that tidal volumes > 700 mL and peak airway pressures > 30 cmH_2O were independently associated with the development of ARDS [7]. In an intraoperative study of patients having esophageal surgery, Michelet et al. [8] compared the use of tidal volumes of 9 mL/kg without positive end-expiratory pressure (PEEP) during two- and one-lung ventilation (OLV) vs. 9 mL/kg during two-lung



Michelet P, et al. Anesthesiology 2006; 105: 911-9

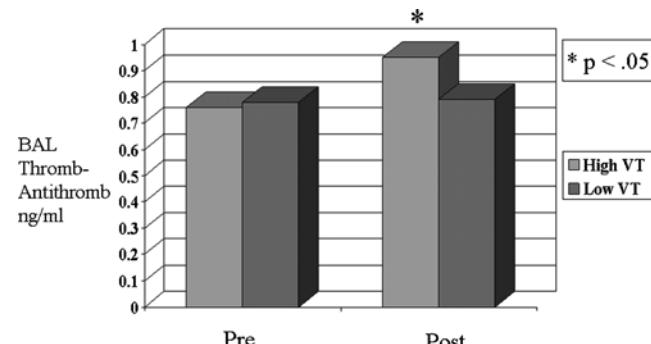
FIG. 10.1. Serum levels of inflammatory cytokine IL-1 β before and after periods of one-lung ventilation (OLV) in patients having esophagectomies. Patients' lungs were ventilated with either a large tidal volume (9 mL/kg) (high VT) or a small tidal volume (5 mL/kg) (low VT) plus PEEP (5 cmH₂O) during OLV. (based on data from Ref. [8]).



Michelet P, et al. Anesthesiology 2006; 105: 911-9

FIG. 10.2. Ratio of arterial oxygen tension to inspired oxygen concentration (PaO₂/FiO₂) in patients ventilated with either a large tidal volume (9 mL/kg) or a small tidal volume (5 mL/kg) plus PEEP (5 cmH₂O) during OLV (based on data from Ref. [8]).

ventilation and 5 mL/kg during OLV with PEEP 5 cmH₂O. They found significantly lower serum makers of inflammation (cytokines IL-1 β , -6 and -8) in the lower tidal volume plus PEEP group (see Fig. 10.1). This study did not find any major difference in postoperative outcome between the two groups; however, it was not powered to do this. The study did demonstrate better oxygenation in the lower tidal volume group during and immediately after OLV (see Fig. 10.2) but not after 18 h. In a study of major abdominal surgery patients ventilated for >5 h, Choi et al. [9] compared the use of 12 mL/kg tidal volumes without PEEP vs. 6 mL/kg plus PEEP 10 cmH₂O. Bronchiolar lavages were performed before and after 5 h of mechanical ventilation. Lavage fluid from the high tidal volume group showed a pattern of leakage of plasma into the alveoli with increased levels of thrombin-antithrombin complexes (see Fig. 10.3), soluble tissue factor, and factor VIIa. This is the hallmark of alveolar lung injury. A clear pattern seems to be appearing from the clinical research that, even in patients with no lung disease, the use of nonphysiologic patterns of ventilation with large tidal volumes and without PEEP causes a degree of systemic inflammation and lung injury.



Choi G, et al. Anesthesiology 2006; 105: 689-95

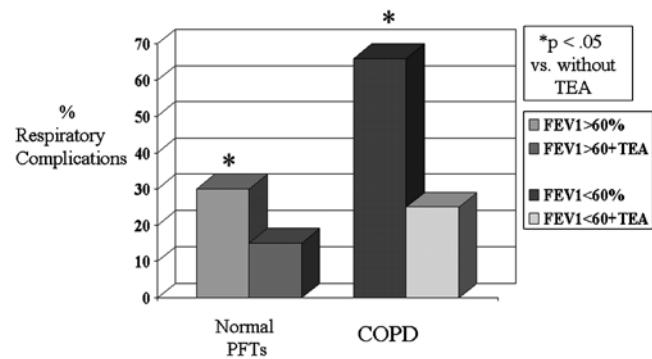
FIG. 10.3. Broncho-alveolar lavage (BAL) levels of thrombin-antithrombin complexes as a marker of lung epithelial injury in patients ventilated for >5 h during abdominal surgery with either a large tidal volume (high VT) (12 mL/kg) without PEEP vs. a small tidal volume (low VT) (6 mL/kg) with PEEP (10 cmH₂O) (based on data from Ref. [9]).

The severity of this injury seems to be directly related to the duration of mechanical ventilation.

Atelectasis is a frequent postoperative complication of surgical procedures. Atelectasis occurs intraoperatively as part of essentially any general anesthetic [10]. Anesthesiologists are aware of this and techniques to avoid it with air-oxygen mixtures, PEEP and recruitment maneuvers are used frequently [11]. However, anesthesiologists are often not aware that atelectasis is a pathological state, and if it persists in the postoperative period leads to increased capillary permeability and an inflammatory response with subsequent lung injury. Atelectasis injures the lung while it is atelectatic due to local release of inflammatory mediators and it injures the lung if the lung is repeatedly subjected to collapse and recruitment [12]. Atelectasis also contributes to injury in the nonatelectatic lung regions, which develop a volutrauma injury due to excessive distribution of inspired volume to these remaining, ventilated, lung regions [13]. Both retrospective [14] and prospective [15] studies have consistently shown that appropriate thoracic epidural analgesia reduces the incidence of respiratory complications (atelectasis, pneumonia, and respiratory failure) after major abdominal and thoracic surgery. The benefits of epidural analgesia seem to be in direct proportion to the severity of the patient's underlying lung disease. Patients with chronic obstructive pulmonary disease (COPD) seem to derive the most benefit from epidural analgesia (see Fig. 10.4). It has also been recently demonstrated that aggressive physiotherapy with CPAP in the postoperative period in patients who develop early desaturation after major abdominal surgery leads to lower rates of major respiratory complications [16].

Pulmonary Resection

There are some situations when the anesthesiologist appreciates that a patient presenting for surgery may have a lung injury (trauma/ARDS, lung transplantation, etc.). However,



Licker M, et al. Ann Thorac Surg 2006; 81: 1830-8

FIG. 10.4. Percent of patients experiencing postoperative respiratory complications in a retrospective study following thoracic surgery for lung cancer. The benefits of thoracic epidural analgesia were more marked in patients with chronic obstructive pulmonary disease (COPD) than in patients with normal preoperative pulmonary function tests (PFTs) (based on data from Ref. [2]).

there are many more cases where the lung injury is subclinical and under-appreciated in the perioperative period (cardiopulmonary bypass, large pulmonary resections [17]). ALI following pulmonary resection has been described since the beginning of OLV for thoracic surgery. The most publicized report is a compilation of ten cases following pneumonectomy published in 1984 [18], which focused on the role of intravenous over-hydration as a cause of postpneumonectomy pulmonary edema. Subsequently, there have been several reviews of this topic identifying a variety of other potentially causative factors for ALI such as the administration of fresh frozen plasma (FFP), mediastinal lymphatic damage, inflammation, and oxygen toxicity [19]. The most thorough study to date [20] is a retrospective survey of 806 pneumonectomies which found 21 cases (2.5%) of postpneumonectomy pulmonary edema, one of the lowest incidences reported of this complication. There were no differences in perioperative fluid balance between postpneumonectomy ALI cases (positive fluid balance at 24 h: 10 mL/kg) vs. matched pneumonectomy controls (13 mL/kg). These authors used rigorous fluid restriction compared to other reports [21] (e.g., 24 h positive balance: 21 ± 9 mL/kg) suggesting that limiting intraoperative fluids might decrease but not eliminate ALI. Further reports demonstrate improved survival from postpneumonectomy pulmonary edema is likely due to improved postoperative management of established cases [22].

Postpneumonectomy ALI [23] has been found to have a bimodal distribution of onset. Late cases (10/37, 27%) presented 3–10 days postoperatively and were secondary to obvious causes such as bronchopneumonia, aspiration, etc. “Primary” ALI (27/37, 73% of cases) presented on postoperative days 0–3. Four factors were independent significant predictors of primary ALI: high intraoperative ventilation pressures, excessive intravenous volume replacement, pneumonectomy, and preoperative alcohol abuse. The known facts

TABLE 10.1. Factors associated with acute lung injury following pulmonary resection.

Large pulmonary resections (right pneumonectomy, extra-pleural pneumonectomy)
Large tidal volumes during OLV (>9 mL/kg ideal body weight)
Excessive intravenous fluids (>20 mL/kg positive fluid balance first 24 h)
Decreased lung function (low predicted postoperative DLCO or FEV1)
Duration of OLV
Preoperative chemotherapy
Restrictive lung disease
Administration of fresh-frozen plasma and other blood products
Age
Preoperative alcohol abuse
DLCO diffusing capacity of the lung for carbon monoxide; FEV1 forced expiratory volume in 1 s

TABLE 10.2. Causes of postresection lung injury.

Probable	Possible
Endothelial injury	Inflammatory response
Epithelial injury (large tidal volumes)	Right ventricular dysfunction (raised CVP)
Increased pulmonary capillary pressure	Oxygen toxicity
Fluid overload	
Lung lymphatic injury	

about ALI following lung surgery include: an incidence of 2–4% following pneumonectomy, greater frequency in right vs. left pneumonectomies, symptomatic onset 1–3 days after surgery, high associated mortality (25–50%), and resistance to standard therapies for pulmonary edema. While ALI occurs following lesser pulmonary resections such as lobectomy it has a much lower mortality rate. Of interest, in eight of nine cases who developed unilateral ALI following lobectomy, the ALI was in the nonoperated (i.e., the ventilated) lung [24].

While there is some association between postoperative ALI with fluid overload, the finding of low/normal pulmonary artery wedge pressures and high-protein edema fluid in affected patients suggests a role of endothelial damage (low-pressure pulmonary edema). Postoperative increases in lung capillary permeability of the nonoperated lung occur after pneumonectomy but not lobectomy [25]. This capillary-leak injury may be due to an inflammatory cascade affecting even the nonoperative lung that is triggered by lung resection and is proportional to the amount of lung tissue resected [26, 27]. Free oxygen radical generation in lung cancer patients is related to the duration of OLV [28].

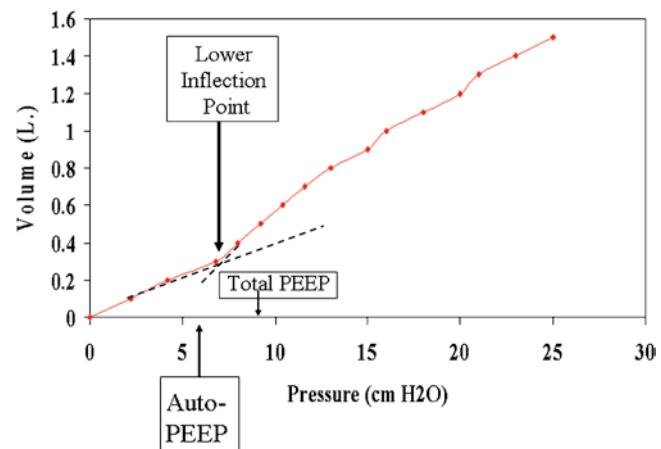
In addition to large tidal volumes and excess intravenous fluids, a wide variety of other factors have been reported to be associated with ALI following pulmonary resection (see Table 10.1) [29]. There is no single mechanism that can fully explain ALI after lung resection and its etiology is likely multifactorial (see Table 10.2). A unifying hypothesis is that postpneumonectomy pulmonary edema is one end of a spectrum of ALI that occurs during all lung resections. The more extensive the resection the more likely there is to be a postoperative injury. The increased dissection and trauma associated with

extra-pleural pneumonectomy places these patients at high-risk to develop postoperative ALI [30]. Also, there may be a genetic predisposition of some patients that increases their risk of developing ALI [31].

Understanding that lung endothelial injury occurs after lung resection supports management strategies similar to other conditions associated with ALI and ARDS. As a general principle, it seems that the lung is least injured when a pattern of ventilation as close as possible to normal spontaneous ventilation can be followed: FiO_2 as low as acceptable, variable tidal volumes [32], beginning inspiration at functional residual capacity (FRC), and avoiding atelectasis with frequent recruitment maneuvers [33]. Studies in ARDS demonstrate that ALI is exacerbated by the use of large tidal volumes and that lung-protective ventilation strategies with low tidal volumes and PEEP are less injurious. The most important factor in the etiology of ventilator-induced lung injury is the end-inspiratory lung volume [34]. Many patients, particularly those with emphysema, develop auto-PEEP during OLV [35] thus beginning inspiration at a lung volume above FRC. It is conceivable that routine use of large tidal volumes (10–12 mL/kg) during OLV in such patients produces end-inspiratory lung volumes close to levels that contribute to ALI.

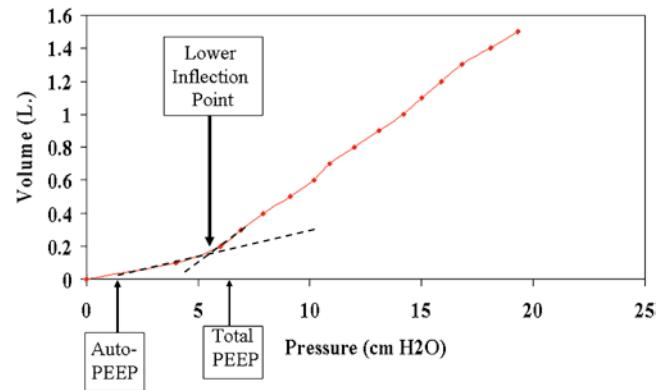
Changes in respiratory function during OLV in the lateral position with an open nondependent hemi-thorax are complex. Initial studies of the application of PEEP during OLV suggested that it led to a deterioration of arterial oxygenation [36]. It is now appreciated that the effects of applied PEEP during OLV depend on the lung mechanics of the individual patient. Most patients with COPD develop auto-PEEP during OLV and thus adding external PEEP leads to hyperinflation and increased shunt (see Fig. 10.5) [37]. However, patients with normal lung parenchyma or those with restrictive lung diseases tend to fall below their FRC at end-expiration during OLV (see Fig. 10.6) and benefit from applied external PEEP [38]. Intraoperative atelectasis may contribute to injury in the dependent lung. It is now appreciated that atelectasis is a pre-inflammatory state predisposing to injury both in the atelectatic portion of the lung and in ventilated regions in the same lung which become hyper-inflated [39].

There is evidence that when an element of lung injury is added to large tidal volume ventilation during OLV, this contributes to ALI. In a rabbit model of OLV during isolated perfusion, large tidal-volume (8 mL/kg) ventilation produced a picture of ALI absent in animals randomized to a lung-protective ventilation pattern (4 mL/kg plus PEEP). Another consideration is management of patients who have received preoperative chemotherapy with agents such as cisplatin and gemcitabine that may affect respiratory function and may increase the risk of postoperative respiratory complications including ALI in some patients [40]. Large pulmonary resections (pneumonectomy or bi-lobectomy) should be considered to be associated with some degree of ALI. ALI, diagnosed radiographically, was reported in 42% of pneumonectomy patients who had been ventilated with peak airway pressures



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FIG. 10.5. The inspiratory compliance curve (lung volume vs. airway pressure) during OLV as the lung is slowly inflated by 100 mL increments in a patient with mild COPD. The lower inflection point of the curve (thought to represent functional residual capacity [FRC]) is at 7 cmH₂O. During OLV this patient developed an intrinsic PEEP (measured by end-expiratory airway occlusion plateau pressure “auto-PEEP”) of 6 cmH₂O. The addition of 5 cm PEEP through the ventilator resulted in a total PEEP in the circuit of 9 cm. The addition of PEEP in this patient raised the end-expiratory lung volume above FRC thus raising pulmonary vascular resistance in the ventilated lung and caused a deterioration in oxygenation (based on data from Ref. [37]).



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FIG. 10.6. The inspiratory compliance curve during OLV in a patient with normal pulmonary function. The lower inflection point of the curve is at 6 cmH₂O. During OLV this patient developed an intrinsic PEEP of 2 cmH₂O. The addition of 5 cm PEEP through the ventilator resulted in a total PEEP in the circuit of 7 cm. The addition of PEEP in this patient raised the end-expiratory lung volume to FRC thus decreasing pulmonary vascular resistance in the ventilated lung and caused an improvement in oxygenation (based on data from Ref. [37]).

>40 cmH₂O [41]. A recent retrospective study found that post-pneumonectomy respiratory failure was associated with the use of higher intraoperative tidal volumes (8.3 vs. 6.7 mL/kg in pneumonectomy patients who did develop respiratory failure) [42]. In a sheep model, Kuzkov et al. demonstrated

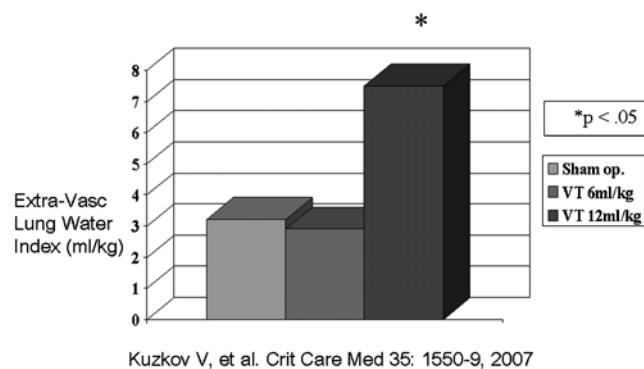


FIG. 10.7. Postmortem extra-vascular lung water index measured by gravimetry after 4 h mechanical ventilation in sheep. Sham op.=control thoracotomy group, no lung resection, tidal volume two-lung ventilation 12 mL/kg. VT 6 mL/kg=pneumonectomy group ventilated with tidal volume (VT) 6 mL/kg+PEEP 5 cm. VT 12 mL/kg=pneumonectomy group ventilated with tidal volume 12 mL/kg, no added PEEP (based on data from Ref. [43]).

that the use of large tidal volume ventilation for 4 h following a pneumonectomy resulted in an increase of extravascular lung water more than double compared to a control (sham operation) group or a pneumonectomy group ventilated with 6 mL/kg tidal volume plus PEEP (see Fig. 10.7) [43].

Since it is not always possible to predict which patient scheduled for a lobectomy may require a pneumonectomy for complete tumor resection, the routine use of several lung protective strategies during OLV seem logical (see Prevention below). It should be appreciated that not all hyperinflation of the residual lung occurs in the operating room. Over-expansion of the remaining lung after a pneumonectomy may occur postoperatively either with or without a chest drain in place. The use of a balanced chest drainage system to keep the mediastinum in a neutral position and avoid hyperinflation of the residual lung following a pneumonectomy has been suggested to contribute to a marked decline in this complication in some centers [44].

The incidence and mortality related to ARDS following pulmonary resection was compared retrospectively for two different time periods (1991–1997 vs. 2000–2005) at a single institution with a large volume of lung surgery [45]. The more recent data showed a decrease in the incidence of ARDS (3.2 vs. 1.6%) and mortality (72 vs. 45%). However, there was no significant decrease in either the incidence (11.4%) or mortality (50%) in ARDS which occurred following pneumonectomy. The main decrease in mortality was secondary to a decrease in the proportion of pneumonectomies as a percentage of the total lung cancer surgical procedures (17.4 vs. 6.4%).

Cardiopulmonary bypass causes a subclinical lung injury that can be aggravated by injurious ventilation patterns (see also Chap. 32). Zupancich [46] compared the use of nonprotective high tidal volumes (10–12 mL/kg) plus low PEEP (2–3 cmH₂O) vs. lung protective low tidal volumes (8 mL/kg) plus high PEEP (10 cmH₂O) in patients ventilated for 6 h

following cardiopulmonary bypass for coronary artery bypass surgery. Serum and bronchiolar lavage levels of the inflammatory cytokines IL-6 and -8 were significantly increased at 6 h only in the nonprotective ventilation group.

Transfusion-Related Acute Lung Injury (TRALI)

Over the past 20 years, ALI secondary to transfusion of blood products has become recognized as a distinct clinical entity. It crosses the boundaries between patients with and without lung injury because it can cause injury to healthy lungs or it can exacerbate incipient lung injury [47]. The etiology of TRALI is primarily due to antiwhite blood cell antibodies in the transfused serum. These antibodies can be to either human leukocyte antigens (HLAs) or human neutrophil antigens (HNAs). Donor HNA antibodies in blood products can bind to and trigger neutrophils and leukocytes in the recipient. HLAs are more widespread and these antibodies can react with white blood cells and/or the pulmonary endothelium of the recipient. Neutrophils normally are flexible and are deformed as they pass through the lung, since the diameter of 50% of the pulmonary capillaries is smaller than the neutrophils. Priming of the neutrophils by sepsis, inflammation or immune triggering (as in the case of TRALI) stiffens the neutrophils which then become sequestered in the pulmonary capillary bed. This process can be aggravated by any physical injury to the endothelium which causes the release of intercellular adhesion molecules which then cause trans-endothelial migration of the sequestered neutrophils into the interstitium of the lung parenchyma, beginning the process of injury (see Fig. 10.8). The process seems to be a two-hit phenomenon usually requiring both: (1) a degree of lung injury, and (2) priming of the circulating neutrophils.

Although TRALI can occur unrelated to surgery, a disproportionate number of cases occur in the perioperative period [48]. Of the commonly used blood products, cryoprecipitate and FFP have the highest rates of antibodies and most associated with the development of both TRALI and ARDS [49]. In trauma cases, the transfusion of >5 U of FFP or >6 U packed red blood cells are independent predictors of developing ARDS. Some partially preventative measures are open to blood bankers such as the use of washed red cells, leukocyte-depleted red cells, and avoiding plasma donations from multiparous females. However, the major burden of prevention falls on the anesthesiologist to avoid unnecessary transfusion of blood products and to decrease the potential for perioperative mechanical lung injury.

Prevention

There are no proven strategies that will prevent postthoracotomy ALI. However given what is known of the pathophysiology, particularly the tendency of the ventilated lung to develop an endothelial injury after major pulmonary resections, and based

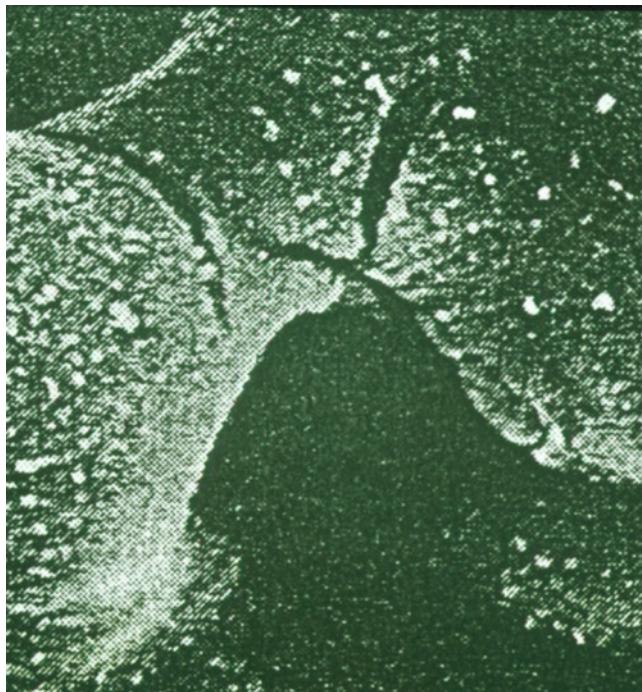


FIG. 10.8. Scanning electron micrograph of a pulmonary capillary from a rabbit lung which has been over-distended by excessive inspiratory volumes and pressure. Full thickness disruptions can be seen in the capillary wall. These stress fractures are the micro-anatomy of volume-induced lung injury and allow circulating neutrophils to be extruded into to the intercellular matrix and alveoli, which may lead to the development of lung injury if the neutrophils are primed by prior exposure to antibodies from a donor transfusion (reprinted from Fu et al. [62] with permission).

on studies of intensive care populations with ARDS several commonsense management approaches seem logical [50].

Applying the principles of lung protective ventilation has been shown to improve outcomes for ARDS patients [51]. The principles of lung protective ventilation are intuitive, you the reader are using lung protective ventilation for yourself at this moment, incorporating: as low an FiO_2 as clinically safe, using small tidal volumes, varying position and tidal volumes, with a small amount of intrinsic PEEP and frequent recruitment maneuvers. If you are yawning it may be from reading this text or it may be that mechanoreceptors in your pulmonary parenchyma have sent a message to your brainstem to recruit areas of micro-atelectasis in the lung, which occurs during normal nonsedated respiration.

Although the principles of lung protective ventilation are straightforward, applying the principles intraoperatively is more complex. A suggested protocol for OLV is presented in Table 10.3. Using smaller tidal volumes (4–5 mL/kg ideal body weight) rather than the traditional large tidal volumes (10–12 mL/kg) for OLV will lead to more atelectasis in the dependent, ventilated, lung unless prophylactic measures are used routinely: PEEP, frequent recruitment maneuvers and the FiO_2 is decreased using air while maintaining a safe level of oxygen

TABLE 10.3. Suggested guidelines for OLV.

Variable	Optimal setting	Exceptions
Tidal volume	4–5 mL/kg	Peak Pa/w <35 Plateau Pa/w <25
PEEP	Total 5 cm	Not added if COPD
FiO_2	1.0	Decrease as tolerated
Respiratory rate	12	Mild hypercapnia OK
Ventilation mode	Vol.-C Vent. or P-C Vent.	P-C Vent.: ESLD, lung transplant, pneumonectomy

Pa/w airway pressure (cm/H₂O); COPD chronic obstructive pulmonary disease; Vol.-C Vent. volume-controlled ventilation; P-C Vent. pressure-controlled ventilation; ESLD end-stage lung disease

saturation. It is not simple, at present, to choose the ideal level of PEEP for an individual patient and it is not possible to reliably measure total-PEEP or auto-PEEP with current anesthesia ventilators. Our current practice is to add 5 cmH₂O PEEP to all patients during OLV except those patients with moderate or severe COPD. The use of pressure-controlled ventilation, vs. the traditional volume-controlled ventilation, has not been clearly shown to be beneficial [52]. However, there is the possibility that regional hyperinflation of lung areas is more likely to occur during inflation with volume-controlled ventilation so it seems to be logical to use pressure-controlled ventilation in patients at increased risk of lung injury such as large pulmonary resections, lung transplantation, or patients with severe chronic lung disease.

Several volatile anesthetic agents have been shown to ameliorate ischemia–reperfusion injury in cardiac surgery compared to intravenous anesthetics [53]. In thoracic surgery, desflurane has been shown to decrease the inflammatory response as measured by assays of cytokines and other pro-inflammatory markers in broncho-alveolar lavage (BAL) fluid from the ventilated lung before and after OLV [54]. Similarly, sevoflurane has been shown to decrease the BAL markers of inflammation in the nonventilated lung following thoracic surgery compared to propofol anesthesia [55]. Neither of these studies were powered to investigate outcomes following anesthesia, however since the inflammatory response exacerbates lung injury it seems to be prudent, at this time, to use volatile anesthesia during thoracic surgery whenever possible.

Excess intravenous fluids tend to accumulate quickly in the dependent lung and will presumably exacerbate any lung injury [56], leading to the clinical maxim “Don’t drown the down lung.” However, there is no clear evidence that moderate amounts of intravenous fluids cause lung injury. A fluid management scheme that limits overall net positive fluid balance in the first 24 h to <20 mL/kg, with no fluid administration for theoretical third space losses and accepting mild oliguria (0.5 mL/kg/h) seems to be an acceptable compromise. There is no reasonable proof to support or refute the use of colloids vs. crystalloids in the thoracic surgery population. Modern synthetic colloids are useful to replace equivalent volumes of lost blood (up to 10–12 mL/kg), potentially avoiding unnecessary small-volume transfusions, in patients who are not anemic.

Since there is an element of capillary injury in ALI it is important to consider and avoid other factors, besides intravenous volume overload, that may increase pulmonary vascular pressure. Such factors include hypoxemia, hypercarbia, and pain.

Therapy for Acute Lung Injury

A number of therapies have been suggested to treat ALI. Randomized placebo-controlled trials of several different therapies including surfactant, prone positioning, inhaled nitric oxide, and anti-inflammatories have not shown significant clinical benefits in patients with established ALI [57]. β -Adrenergic agents are generating much interest as a potential treatment for ALI [58]. β -Agonists increase the rate of alveolar fluid clearance by increasing cellular cyclic adenosine monophosphate (cAMP) in the epithelium, also β -agonists have anti-inflammatory properties. In a randomized placebo-controlled study in 40 patients with ALI, Perkins et al. [59] found that the use of intravenous salbutamol decreased lung water and plateau airway pressure, although there were no significant differences in outcome. A randomized study of inhaled salmeterol has shown that it can reduce the incidence of high-altitude pulmonary edema in subjects at risk [60].

Extra-pulmonary ventilation has been reported for ARDS after pulmonary resection [61]. Seven patients (five pneumonectomy, two lobectomy) were treated for severe ARDS post-pulmonary resection, refractory to conventional therapy, with an interventional lung-assist device (Novalung GmbH, Hechingen, Germany) (see also Chap. 43). During the period of lung-assist (mean duration 4 days), the conventional mechanical ventilation was decreased to extremely low levels (mean FiO_2 0.5, tidal volume 3 mL/kg, respiratory rate 6 breaths/min) and six of seven (86%) of the patients survived. Although this is a very small series, the results are encouraging in a patient population that has a mortality that usually approaches 50%.

Clinical Case Discussion

A 55-year-old 70 kg male presents with bronchogenic carcinoma of the right middle and lower lobes. The patient is a smoker (30 pack-year) with good exercise tolerance. Preoperative $\text{FEV}_1 = 80\%$ predicted and $\text{DLCO} = 70\%$ predicted. V/Q scan shows 50% ventilation and perfusion to the right lung. The patient has an uncomplicated 3 h right pneumonectomy. During the procedure he receives 1.5 L of crystalloid and is ventilated with a tidal volume of 700 mL, FiO_2 1.0, during both two- and one-LV. Postoperatively, the patient is stable in the recovery room (see Fig. 10.9) with thoracic epidural analgesia and is discharged to the thoracic surgical floor.

On postoperative day 3, the patient complains of increasing dyspnea. The patient's oxymetric saturation is 85% on air and 93% with FiO_2 0.4 mask. His pulse is sinus rhythm at 104 and blood pressure 130/80. A repeat chest X-ray is taken (see Fig. 10.10)

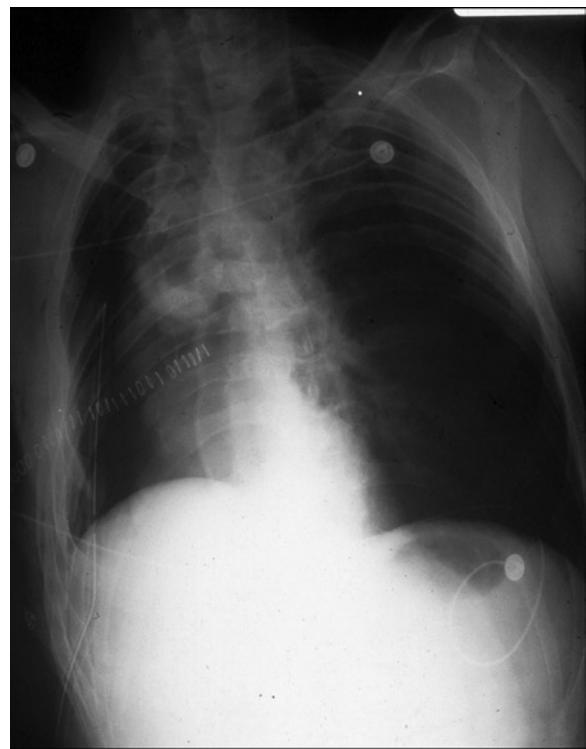


FIG. 10.9. Immediate postoperative chest X-ray of a 55-year-old male following a right pneumonectomy. This is normal postpneumonectomy film.



FIG. 10.10. Chest X-ray on postoperative day 3 of the same patient as Fig. 10.9. The patient has gradually become more dyspneic and has significant arterial oxygen desaturation breathing air. Chest X-ray shows signs of increased lung interstitial markings suggestive of pulmonary edema.

- What is the differential diagnosis?
- How can the diagnosis be confirmed?

The differential should include postthoracotomy ALI, pulmonary embolus, congestive heart failure and/or myocardial ischemia, aspiration and pneumonia. ALI in this setting is a diagnosis of exclusion. A perfusion lung scan should be obtained to rule-out emboli and an electrocardiogram to rule out subclinical ischemia, which is unlikely in the absence of a prior history of coronary heart disease or diabetes. A transthoracic echocardiogram should be performed to rule out myocardial dysfunction. Major aspiration is unlikely without a history of a decreased level of consciousness. Pneumonia is a possibility, but unlikely without signs of sepsis or an elevated white blood cell count, sputum for culture and sensitivity should be obtained. If other common possibilities of postoperative respiratory failure are ruled out, the provisional diagnosis is ALI.

- What therapy is indicated?

The patient should be transferred to an intensive care unit. All therapy is basically palliative with the aim to support respiratory function and minimize any exacerbation of the lung injury pending spontaneous resolution. Initially respiratory support should begin with noninvasive ventilation and minimizing the FiO_2 to maintain normal physiologic oxygen saturations. Attempts to reduce the pulmonary vascular pressures with inhaled nitric oxide or prostacyclin are logical although not proven and are unlikely to cause harm. The same applies to inhaled β -adrenergic agents. The benefit of corticosteroids is uncertain. If gas exchange deteriorates, then mechanical ventilation using the principles of lung protection will need to be added. In severe ALI, unresponsive to conventional therapy, the use of extra-pulmonary ventilation should be considered.

References

1. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. *Am J Respir Crit Care Med.* 1994;149:818–24.
2. Licker M, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg.* 2006;81:1830–8.
3. Alam N, Park BM, Wilton A, et al. Incidence and risk factors for lung injury after lung cancer resection. *Ann Thorac Surg.* 2007;84:1085–91.
4. Bendixen HH, Hedley-White J, Laver MB. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation: a concept of atelectasis. *N Engl J Med.* 1963;96:156–66.
5. Tenny SM, Remmers JE. Comparative quantitative morphology of the mammalian lung: diffusing area. *Nature.* 1963;197:54–6.
6. Gajic O, Dara SI, Mendez JL, et al. Ventilator associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. *Crit Care Med.* 2004;32:1817–24.
7. Gajic O, Frutos-Vivar F, Esteban A, et al. Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. *Intens Care Med.* 2005;31:922–6.
8. Michelet P, D'Journo X-B, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy. *Anesthesiology.* 2006;105:911–9.
9. Choi G, Wolthuis EK, Bresser P, et al. Mechanical ventilation with lower tidal volumes and positive end-expiratory pressure prevents alveolar coagulation in patients without lung injury. *Anesthesiology.* 2006;105:689–95.
10. Lindberg P, Gunnarsson L, Tokics L, et al. Atelectasis and lung function in the postoperative period. *Acta Anaesthesiol Scand.* 1992;36:546–53.
11. Tusman G, Bohm SH, Suarez-Sipmann F. Alveolar recruitment improves ventilatory efficiency of the lungs during anesthesia. *Can J Anesth.* 2004;51:723–7.
12. Duggan M, Kavanagh B. Pulmonary Atelectasis a pathological perioperative entity. *Anesthesiology.* 2005;102:838–54.
13. Tsuchida S, Engelberts D, Peltekova V, et al. Atelectasis causes alveolar injury in nonatelectatic lung regions. *Am J Resp Crit Care Med.* 2006;174:279–89.
14. Ballantyne JC, Carr DB, deFerranti S. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analysis of randomized, controlled trials. *Anesth Analg.* 1998;86:598–612.
15. Rigg J, Jamrozik K, Myles P, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomized trial. *Lancet.* 2002;359:1276–82.
16. Squadrone V, Coha M, Cerutti E, et al. Continuous positive airway pressure for treatment of postoperative hypoxemia. *JAMA.* 2005;293:589–95.
17. Grichnik KP, D'Amico TA. Acute lung injury and acute respiratory distress syndrome after pulmonary resection. *Sem Cardiothorac Vasc Anesth.* 2004;8:317–34.
18. Zeldin RA, Normandin D, Landtwing BS, Peters RM. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg.* 1984;87:359–65.
19. Slinger P. Post-pneumonectomy pulmonary edema: is anesthesia to blame? *Curr Opin Anesthesiol.* 1999;12:49–54.
20. Turnage WS, Lunn JL. Postpneumonectomy pulmonary edema. A retrospective analysis of associated variables. *Chest.* 1993;103:1646–50.
21. Waller DA, Gebitekin C, Saundres NR, Walker DR. Noncardiogenic pulmonary edema complicating lung resection. *Ann Thorac Surg.* 1993;55:140–3.
22. Keegan MT, Harrison BA, De Ruyter ML, Deschamps C. Post-pneumonectomy pulmonary edema are we making progress? *Anesthesiology.* 2004;101:A431.
23. Licker M, De Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97:1558–65.
24. Padley SPG, Jordan SJ, Goldstraw P, et al. Asymmetric ARDS following pulmonary resection. *Radiology.* 2002;223:468–73.
25. Waller DA, Keavey P, Woodfine L, Dark JH. Pulmonary endothelial permeability changes after major resection. *Ann Thorac Surg.* 1996;61:1435–40.
26. Williams EA, Quinlan GJ, Goldstraw P, et al. Postoperative lung injury and oxidative damage in patients undergoing pulmonary resection. *Eur Respir J.* 1998;11:1028–34.
27. Tayama K, Takamori S, Mitsuoka M, et al. Natriuretic peptides after pulmonary resection. *Ann Thorac Surg.* 2002;73:1582–6.
28. Misthos P, Katsaragikis A, Milingos N, et al. Postresectional pulmonary oxidative stress in lung cancer patients. The role of one-lung ventilation. *Eur J Cardiothorac Surg.* 2005;27:379–83.

29. Licker M, Fauconnet P, Villiger Y, et al. Acute lung injury and outcomes after thoracic surgery. *Curr Opin Anaesthesiol*. 2009;22:61–7.
30. Stewart DJ, Martin-Uncar AE, Edwards JG, et al. Extra-pleural pneumonectomy for malignant mesothelioma: the risks of induction chemotherapy, right-sided procedures and prolonged operations. *Eur J Cardiothorac Surg*. 2005;27:373–8.
31. Marzec JM, Christie JD, Reddy SR, et al. Functional polymorphisms in the transcription factor NRF2 in humans increase the risk of acute lung injury. *FASEB J*. 2007;21:2237–46.
32. Boker A, Haberman C, Girling L, et al. Variable ventilation improves perioperative lung function in patients undergoing abdominal aortic aneurysmectomy. *Anesthesiology*. 2004;100:608–16.
33. Mols G, Priebe H-J, Guttmann J. Alveolar recruitment in acute lung injury. *Br J Anaesth*. 2006;96:156–66.
34. Dreyfuss D, Soler P, Basset G, et al. High Inflation pressure pulmonary edema. *Am Rev Resp Dis*. 1988;137:1159–64.
35. Slinger P, Hickey DR. The interaction between applied PEEP and auto-PEEP during one-lung ventilation. *J Thorac Cardiovasc Anesth*. 1998;12:133–6.
36. Capan LM, Turndorf H, Patel C, et al. Optimization of arterial oxygenation during one-lung anesthesia. *Anesth Analg*. 1980;59:847–51.
37. Slinger P, Kruger M, McRae K, Winton T. Relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung. *Anesthesiology*. 2001;95:1096–102.
38. Fujiwara M, Abe K, Mashimo T. The effect of positive end-expiratory pressure and continuous positive airway pressure on the oxygenation and shunt fraction during one-lung ventilation with propofol anesthesia. *J Clin Anesthesia*. 2001;13:473–7.
39. Tsuichida S, Engleberts D, Peltekova V, et al. Atelectasis causes alveolar injury in nonatelectatic lung regions. *AJRCCM*. 2006;174:279–89.
40. Leo F, Solli P, Spaggiari L, et al. Respiratory function changes after chemotherapy: an additional risk for post-operative respiratory complications? *Ann Thorac Surg*. 2004;77:260–5.
41. Van der Werff YD, van der Houwen HK, Heilmans PJM, et al. Postpneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest*. 1997;111:1278–84.
42. Fernandez-Perez E, Keegan M, Brown DR. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology*. 2006;105:14–8.
43. Kuzkov V, Subarov E, Kirov M. Extravascular lung water after pneumonectomy and one-lung ventilation in sheep. *Crit Care Med*. 2007;35:1550–9.
44. Alvarez JM, Panda RK, Newman MAJ, et al. Postpneumonectomy pulmonary edema. *J Cardiothorac Vasc Anesth*. 2003;17:388–95.
45. Tang SSK, Redmond K, Griffiths M, et al. The mortality from acute respiratory distress syndrome after pulmonary resection is reducing. *Eur J Cardiothorac Surg*. 2008;34:898–902.
46. Zupancich E. Mechanical ventilation affects inflammatory mediators in patients undergoing cardiopulmonary bypass for cardiac surgery: a randomized controlled trial. *J Thorac Cardiovasc Surg*. 2005;130:378–83.
47. Bux J, Sachs UJH. The pathogenesis of transfusion related lung injury (TRALI). *Br J Haematol*. 2007;136:788–99.
48. Popovsky MA, Moore SB. Diagnostic and pathogenic considerations in transfusion-related acute lung injury. *Transfusion*. 1985;25:573–7.
49. Chaiwat O, Lang JD, Vavilala MS, et al. Early packed red blood cell transfusion and acute respiratory distress syndrome after trauma. *Anesthesiology*. 2009;110:351–60.
50. Lytle FT, Brown DR. Appropriate ventilator settings for thoracic surgery: intraoperative and postoperative. *Sem Cardiothorac Vasc Anesth*. 2008;12:97–108.
51. Yilmaz M, Gajic O. Optimal ventilator settings in acute lung injury and acute respiratory distress syndrome. *Eur J Anaesthesiol*. 2008;25:89–96.
52. Unzueta MC, Casas JI, Moral MV. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation for thoracic surgery. *Anesth Analg*. 2007;104:1029–33.
53. De Hert S, ten Broecke PW, Mertens E, et al. Sevoflurane but not propofol preserves myocardial function in coronary surgery patients. *Anesthesiology*. 2002;97:42–9.
54. Schilling T, Kozian A, Kretzschmar M, et al. Effects of desflurane or propofol on pulmonary and systemic immune responses to one-lung ventilation. *Br J Anaesth*. 2007;99:368–75.
55. De Conno E, Steurer M, Wittlinger M, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *Anesthesiology*. 2009;110:1316–26.
56. Jefferson RF, Leon Y, Moallem S, et al. Immobility, hypoxemia and pulmonary arteriovenous shunting. *Arch Surg*. 1974;109:537–41.
57. Bernard GR. Acute respiratory distress syndrome. *Am J Resp Crit Care Med*. 2005;171:1125–8.
58. Matthay M. β -adrenergic agonist therapy as a potential treatment for acute lung injury. *Am J Resp Crit Care Med*. 2006;173:254–5.
59. Perkins GD, McAuley DF, Thickett DR, et al. The β -agonist lung injury trial. *Am J Resp Crit Care Med*. 2006;173:281–7.
60. Sartori C, Allemann Y, Duplain H, et al. Salmeterol for the prevention of high altitude pulmonary edema. *N Eng J Med*. 2002;346:1631–6.
61. Iglesias M, Martinez E, Badia JR, et al. Extrapulmonary ventilation for unresponsive severe acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg*. 2008;85:237–44.
62. Fu Z et al. High lung volume increases stress failure in pulmonary capillaries. *J Appl Physiol*. 1992;73:123–33.

11

Bronchoscopic Procedures

Gordon N. Finlayson and Bevan G. Hughes

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Key Points

- Diagnostic flexible bronchoscopy is safely performed outside of the operating room with light to moderate sedation and topical anesthesia.
- Rigid bronchoscopy is typically performed in patients with central airway obstruction and major comorbidities. Primary concerns include the risk of complete airway obstruction and inability to ventilate or dynamic hyperventilation with hemodynamic compromise.
- A fluid transition between novel ventilation strategies is often required for these procedures.
- Multimodal techniques employed by interventional bronchoscopists to acutely re-establish patency of obstructed central airways include: stenting, laser, endobronchial electrosurgery, argon plasma coagulation, and balloon bronchoplasty.
- Major intraoperative complications associated with these techniques include hemorrhage, airway trauma, perforation, fire, systemic gas embolism, and dissemination of postobstructive pneumonia.
- Alternative indications for these procedures include treatment of low-grade malignancies and carcinoma in situ. These lesions may also respond to brachytherapy, cryotherapy, or photodynamic therapy.
- Interventional bronchoscopy is an evolving field with expanding applications. Future indications may include endobronchial valve insertion for persistent air leaks and COPD as well as bronchial thermoplasty for treatment-resistant asthma.

Introduction

Routine diagnostic flexible bronchoscopy is a well-established, safe procedure that rarely demands the presence of an anesthesiologist. Interventional bronchoscopy is an evolving, specialized discipline that has a pivotal role in the strategic relief of central airway obstruction and the anastomotic complications of lung transplantation. Many of these procedures require general anesthesia and provide significant challenges in establishing a patent airway and maintaining adequate ventilation. There are a number of newer interventions adopted by bronchoscopists for management of precancerous lesions and early-stage malignancies. Emerging roles for interventional pulmonologists include minimally invasive lung volume reduction with placement of endobronchial valves and bronchial thermoplasty for severe asthma.

Anesthetic Considerations

Therapeutic bronchoscopic interventions have historically been aimed at the relief of airway obstruction using a rigid endoscope. The first reported use of bronchoscopy by Gustav Killian in 1897 was for the removal of a right mainstem foreign body. Soon thereafter, attempts were aimed at resection of tumor, dilation of infectious strictures, and drainage of obstructive secretions [1].

Rigid bronchoscopy involves the placement of a noncuffed, straight metal endoscope directly into the trachea, precluding the placement of an endotracheal tube. This is a key

distinction when compared to flexible bronchoscopy which can be performed on an intubated patient with a secured airway. Rigid rather than flexible bronchoscopy is most commonly used for interventional procedures, as it allows for the passage of large instruments, removal of bulky objects while simultaneously providing a patent airway for provision of positive pressure ventilation (Table 11.1).

During rigid bronchoscopy gas exchange is most commonly maintained by jet ventilation as the open-circuit design renders conventional positive pressure ventilation prone to gas leak. Using a handheld injector or high-frequency jet ventilator, high-flow oxygen at variable concentrations can be delivered to the lungs. The precise fraction of inspired oxygen achieved is somewhat less than that selected on the injector because entrainment of room air ultimately dilutes the delivered oxygen content. Similarly, the use of volatile agents is unreliable because its delivery and measurement cannot be guaranteed. Since the breathing circuit is not sealed, leakage of anesthetic gas also contaminates the operating room. Jet injection of a blended oxygen/air mixture is typically delivered through high-pressure tubing connected either directly to an intraluminal port incorporated in the bronchoscope, or to a catheter placed within the airway.

Various other ventilation strategies are also available during rigid bronchoscopy though these may be more challenging to perform effectively. Spontaneous breathing is an option [2], however many bronchoscopists insist on paralysis as unanticipated coughing or straining may lead to increased technical challenges and complications. Placement of a rigid bronchoscope requires considerable neck extension and extensive manipulation of the airway such that most patients are intolerant without inducing apnea. There are ventilating bronchoscopes available that are designed to allow the use of an anesthetic breathing circuit, however these mandate closely matching the size of the bronchoscope with the trachea, to prevent gas leakage [87]. Theoretically it is possible to provide conventional ventilation in this circumstance, but any significant leak would reduce the efficacy of this technique. Finally, with judicious preoxygenation and passive insufflation of oxygen, short periods of apnea are generally well

tolerated in select patients. For procedures requiring extended airway manipulation, this strategy may be interrupted intermittently to provide positive pressure ventilation.

Anesthetic considerations for interventional bronchoscopy include the operative indication, patient comorbidities, and appreciation of procedure-specific complications. Airway obstruction remains the most common indication requiring bronchoscopic intervention and these procedures are typically performed urgently or emergently on physiologically distressed patients [3]. Ultimately, this may lead to conflicting anesthetic goals including balancing a full stomach with an unsecured airway, high oxygen requirements with the risk of fire ignition, and jet ventilation through obstructing stenoses with the risk of air trapping and barotrauma (Table 11.2).

Total intravenous anesthesia (TIVA) avoids operating room contamination with inhalational agents during interventional bronchoscopy [4] (see Chap. 12). Another advantage of intravenous agents is avoiding the dependence of anesthetic delivery on ventilation – an important consideration when novel ventilation strategies are anticipated. Standard monitors recommended by the American Society of Anesthesiologists are mandatory for interventional procedures. Arterial cannulation or transcutaneous pCO_2 monitoring is useful for assessing the adequacy of gas exchange because of the frequent interruption to end-tidal carbon dioxide sampling. Patients receiving TIVA and muscle relaxants are at higher risk for awareness, therefore extended monitoring (e.g., BIS) and the addition of benzodiazepines may be considered. As the presence of an intratracheal instrument is a strong stimulator of cough, patients almost invariably require paralysis. Including a potent, short-acting opioid (e.g., remifentanil) in the TIVA regimen can help suppress this powerful and disruptive reflex. Given the unique and potentially unanticipated technical challenges presented by these cases, an extended procedural duration may require ongoing neuromuscular blockade with close monitoring of depth of paralysis.

TABLE 11.2. Anesthetic considerations of rigid bronchoscopy.

Flexible bronchoscopy	Rigid bronchoscopy
Minimal sedation	Requires general anesthesia
May be used through endotracheal tube	Difficult with endotracheal tube <i>in situ</i>
No absolute contraindications	Cervical spine pathology contraindicated
Minimal risk of trauma	Significant risk of trauma
Inability to ventilate through scope (excluding HFJV)	Provides airway for ventilation
Requires small instruments	May use larger instruments
May need to remove scope when extracting specimen	Able to remove large objects through scope
Can access distal airways	Limited to central airways
Technically straightforward	Specialized training required

1. *Stimulating*
 - Likely require general anesthesia
 - \pm Neuromuscular blockade
2. *Unprotected airway*
 - Aspiration risk
 - Potentially challenging ventilation
 - Potential for loss of airway access
3. *Considerations of jet ventilation*
 - Potential for barotrauma
 - Inability to measure end-tidal CO_2 and hypercapnea
4. *Technical considerations*
 - Shared airway with bronchoscopist
 - Open circuit: room contamination with volatile anesthetic
 - Need for total intravenous anesthesia
5. *Potential for procedure specific complications*
 - Airway fire
 - Hemorrhage
 - Gas embolism
 - Traumatic injuries

Complications of rigid bronchoscopy including airway and dental trauma usually occur during placement of the scope. The potential for difficulties in tracheal intubation must be kept in mind as this may result in a catastrophic inability to ventilate the patient, specifically in those with difficult anatomy or supraglottic distortion. Often these procedures are performed in nonoperative settings; these unfamiliar surroundings have been shown to be a factor in increasing the risk of adverse events [5]. Emergency equipment should include alternatives to direct laryngoscopy and possibly setup for invasive or surgical airway access. Other complications associated with specific interventional bronchoscopic procedures include airway fire, air embolism, and severe hemorrhage; these are discussed in more detail in the remainder of the chapter.

Central Airway Obstruction

Central airway obstruction may originate from intrinsic, extrinsic, or mixed lesions (Fig. 11.1) [6]. These lesions are further characterized by location (intrathoracic vs. extrathoracic), etiology (malignant vs. nonmalignant) (Table 11.3), and presence of fixed or dynamic airflow obstruction [7]. Specific interventional strategies for alleviating an obstruction are dictated by these features and considered within the context of the patient's appropriate level of care. Generally speaking, the comorbidities of these patients reflect the predisposing risks of the underlying malignancy, extrapulmonary features of an associated systemic inflammatory disease or post-transplant status. Because central airway obstructions often progress insidiously, symptoms of dyspnea, wheeze or stridor only manifest with advanced (5–8 mm) lesions [8]. Still, lesions that rapidly encroach upon the airway or involve long segments may prove symptomatic with lesser degrees of obstruction.

Owing to its relative infancy, the perioperative risks of therapeutic bronchoscopy for the relief of central airway obstruction are not clearly defined. Although interventional bronchoscopy may efficiently re-establish patency

of an obstructed airway, data from high volume centers underscore the vigilance demanded in caring for these patients. Approximately 20% of patients will experience perioperative complications with an overall 30-day mortality of 7.8% (primarily attributed to underlying disease progression) [3].

Evaluation of patients with central airway obstruction is largely determined by clinical status and degree of physiologic compromise. Excluding those with impending respiratory arrest, the nature and extent of obstruction must be clearly defined [9]. Traditionally, evaluation with flow volume loops has been advocated. While considered crucial in the assessment of patients suspected of central airway obstruction, their value in preoperative planning is limited [10]. Furthermore, performance of spirometry may provoke respiratory failure in advanced obstructions [11]. Reconstructed, multislice, CT scans of the airway convey crucial information regarding location, extent, dynamic collapse and invasion of adjacent structures that is paramount for safe preoperative planning [12–15]. If demanded by the patient's symptoms, CT scanning may be performed in the prone position.

Owing to the clinical urgency of these cases, the opportunity for optimization of medical comorbidities is limited. Depending upon the indication for intervention, several comorbidities including tobacco use, hypertension, moderate to severe COPD, and diabetes have been associated with increasing the likelihood of complications including bleeding and hypoxemia [3]. Although yet unproven to influence perioperative outcomes for these types of cases, attentive management of co-existing illnesses seems prudent. Preoperatively, selective use of antisialogogues [16] is beneficial for facilitating airway topicalization and fibroscopic examination. Steroids are advocated when repeated instrumentation of the airway threatens postoperative glottic edema [17]. In patients with respiratory distress, heliox (gas mixtures of helium and oxygen, usually with an FiO_2 approximately 30%) can temporarily reduce work of breathing and improve gas exchange when the obstruction causes turbulent airflow [18].

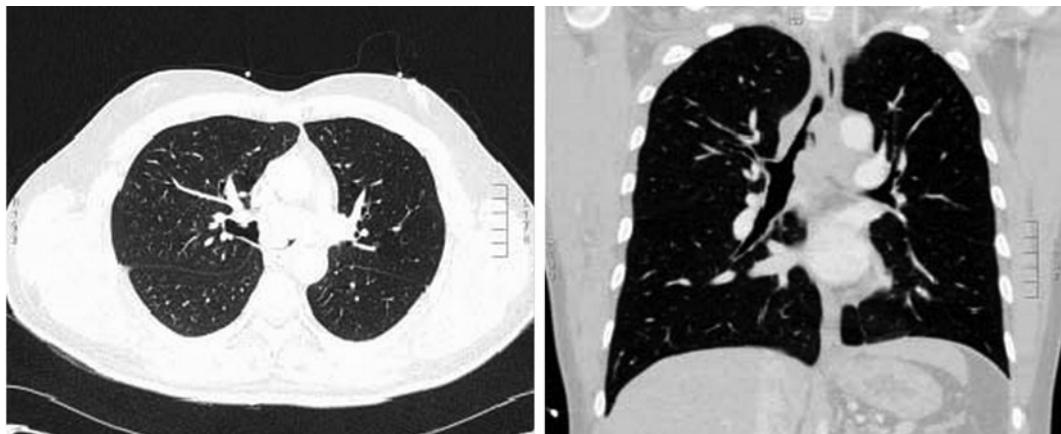


FIG. 11.1. CT demonstrating severe intrinsic central airway obstruction involving the tracheal carina and left main bronchus.

TABLE 11.3. Causes of central airway obstruction.

Benign
<i>Traumatic</i> : post intubation; blunt, penetrating or inhalational injury
<i>Inflammatory</i> : Wegener's; amyloidosis; SLE
<i>Infectious</i> : papillomas; tuberculosis; rhinoscleroma; viral tracheobronchitis; bacterial tracheitis; diphtheria
<i>Vascular</i> : rings; aneurysms; post pneumonectomy syndrome; anomalies (e.g., right innominate artery; double aortic arch)
<i>Neoplastic</i> : neurofibroma, chondroma, chondroblastoma, hemangioma, pleomorphic adenoma
<i>Anastamotic</i> : lung transplant; sleeve resection
<i>Other</i> : tracheomalacia; relapsing polychondritis; sarcoidosis; foreign body
Malignant
<i>Primary malignancy intraluminal</i>
Adenoid cystic
Carcinoid
Mucoepidermoid
Bronchogenic
<i>Primary malignancy extraluminal</i>
Esophageal
Mediastinal (thymus, thyroid, germ cell)
Lymphoma
Sarcoma
<i>Metastatic malignancy</i>
Bronchogenic
Renal Cell
Breast
Thyroid
Melanoma
Colon

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Of foremost concern in managing patients with central airway lesions is the threat of precipitating complete obstruction with routine induction of general anesthesia. Critical central obstructions may also contribute to dynamic hyperinflation and cardiovascular compromise [16]. Because there is a paucity of literature to guide critical decisions in these challenging patients, strategies for the provision of safe anesthesia depend heavily on experience and judgment.

Traditional teaching advocates anesthetic techniques that maintain spontaneous ventilation during acute obstruction in order to avoid airway collapse after paralysis of respiratory musculature [19]. However, experienced centers have documented successful management with intravenous induction and neuromuscular blockade in patients with stridor at rest [20]. Similarly, case series attest to the safe application of innovative ventilation strategies during interventional bronchoscopy [21]. Effective ventilation may be maintained with intermittent, assisted, positive pressure delivered through the side-arm adapter of a rigid bronchoscope. The Sanders technique of manual jet ventilation also provides uninterrupted ventilation delivered through the rigid bronchoscope [22]. High-frequency jet ventilation demonstrates reliable gas exchange and operative conditions without relying on the presence of a rigid bronchoscope [21]. Finally, for those patients with reversible illnesses and critically obstructive lesions, selected use of extracorporeal membrane oxygenation may be justified

[23, 24]. Unfortunately, there are limited data comparing the effectiveness and safety of these ventilation techniques during therapeutic endoscopy [25]. Whichever technique is employed, attention should be dedicated to reassessing the adequacy of ventilation and presence of dynamic hyperinflation throughout the procedure. Oftentimes these cases demand dynamic decision making and flexible transition between various modes of ventilation – preparation is crucial.

The fundamental components to the safe relief of a central airway obstruction include a wide selection of rigid bronchoscopes and a veteran endoscopist to immediately access the airway. Although few general respirologists maintain competency in rigid bronchoscopy [26], many interventional pulmonologists are highly qualified [27]. If there is an anticipated potential for an emergent thoracotomy, the presence of a thoracic surgeon is mandatory. Blind tracheal intubation in patients with central airway lesions should be avoided as it risks precipitating hemorrhage or airway obstruction from unnecessary trauma. Routine use of flexible bronchoscopy will help minimize these complications.

Successful bronchoscopic management of central airway lesions often mandates multimodal techniques. The following sections will highlight these techniques and specific anesthetic considerations.

Airway Stents

Montgomery pioneered the application of airway stents for the management of subglottic stenosis in the 1960s [28]. In 1990, Dumon introduced a silicone stent positioned completely within the tracheal lumen [29]. Today, the armamentarium of interventional bronchoscopists includes a wide selection of stents aimed at restoring the patency of obstructed airways. Generally speaking, modern stents are composed of silicone, metal or combination thereof. Ideally, an airway stent should demonstrate: easy insertion and removal; stability within the airway limiting the tendency for migration; durability to compressive forces and sufficient elasticity to conform to the airway; resistance to granuloma formation and infection and preservation of mucociliary transport [17, 30].

Currently there are no manufactured stents that satisfy these demanding design properties, though innovations in stent technology continue to progress (Fig. 11.2) [31]. Silicone stents are suitable for benign diseases of the central airways because of their ease of removal. Limitations of silicone stents include migration, obstruction with secretions, flammability and reduced inner diameter [32]. Both bare metal stents and covered metal stents are available (Fig. 11.3) (Table 11.4). Advantages of metal stents include preservation of mucociliary transport, large inner diameter, and relatively easier placement. The Achilles' heel of metal stents remains their tendency towards granuloma formation. Additionally, bare metal stents can transmit laser energy and injury surrounding tissue, while covered versions may pose a fire risk during laser procedures [33, 34]. Because of concerns surrounding in-stent obstruction and complicated removal, experts suggest that metal stent

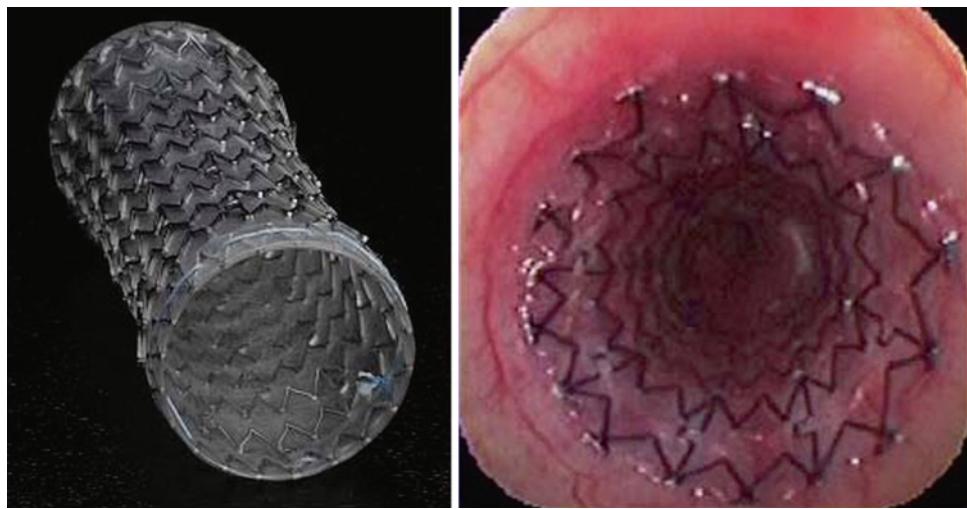


FIG. 11.2. This AERO stent represents the most contemporary design integrating the best features of silicone and metal (image courtesy of Alveolus).



FIG. 11.3. Example of covered and uncovered varieties of expandable metal stents (image courtesy of Boston Scientific).

insertion should be reserved for malignant or palliative situations [35, 36]. Despite this consideration, other authors report successful management of benign conditions with application of metal stents, though thoughtful patient selection is crucial [37, 38].

Deployment of silicone stents requires the use of rigid bronchoscopy. Metal stents can be positioned in the airway using flexible bronchoscopy or fluoroscopy (Fig. 11.4). Primary

TABLE 11.4. Stent properties.

Metal
<i>Advantages</i>
Large inner to outer diameter ratio
Resistant to migration
Preserved mucociliary clearance
May be placed under local anesthesia
<i>Disadvantages</i>
Prone to granulation and restenosis
Transmission of laser energy
Flammable when covered
Risk of long-term airway perforation
Difficult removal (<i>considered permanent</i>)
Silicone
<i>Advantages</i>
Easily repositioned and extracted
<i>Disadvantages</i>
Requires rigid bronchoscopy
Reduced inner to outer diameter ratio
Prone to migration
Inhibition of mucociliary clearance
Secretion impaction
Flammable

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anesthetic considerations for airway stenting overlap with the guiding principles of managing central airway lesions. During stent placement, maintenance of an immobile surgical field is preferred. Strategies to avoid coughing, including judicious airway topicalization, are advocated to minimize the risk of stent dislodgment. Specific intraoperative complications include airway hemorrhage, obstruction, and perforation with resultant pneumothorax or pneumomediastinum. When relieving a chronic airway obstruction, positioning maneuvers to minimize dissemination of a postobstructive pneumonia are recommended [12, 39]. Major chronic complications of airway

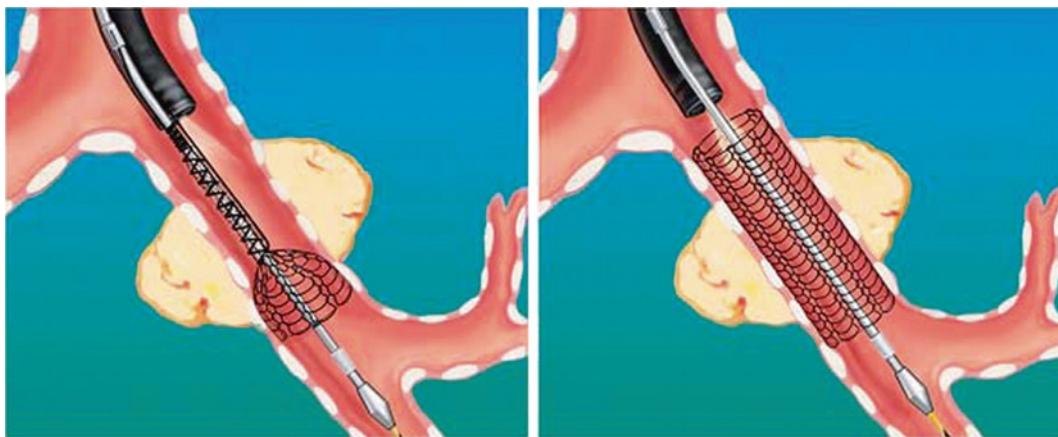


FIG. 11.4. Illustration demonstrates flexible bronchoscopic deployment of expandable metal stent (images courtesy of Boston Scientific).

stents include fistula formation to adjacent structures, which may lead to massive hemoptysis as a result of a bronchovascular fistula or aspiration pneumonia due to an esophagorespiratory fistula [40].

In instances where anesthesia may be required in patients with remote airway stenting, preoperative evaluation should consider the possibility of stent migration or obstruction from secretions, granuloma formation or tumor invasion. Generally speaking, airway instrumentation should be avoided in these patients, with preference given to regional anesthesia if feasible. For general anesthesia, use of a laryngeal mask avoids stent disruption [41]. When tracheal intubation is indicated, fibreoptic inspection of the airway should guide tube placement proximal to (preferred) or within the stent lumen and should be repeated upon extubation [29, 42].

Other Modalities

Since the advent of flexible bronchoscopy as a diagnostic tool in the 1960s, there has been a push to use this versatile instrument for therapeutic purposes as well. Contemporary indications for therapeutic bronchoscopy extend beyond providing relief of acute central airway obstruction. The innovative techniques of interventional bronchoscopists have facilitated new opportunities for palliation of intraluminal obstructing lesions and curative resection of early-staged cancers. Often these bronchoscopic interventions are used in concert with external beam radiation or chemotherapy to facilitate surgical debulking (Fig. 11.5).

Laser

Laser technology involves the focused synchronization of light at a specific wavelength to induce thermal changes leading first to photocoagulation and ultimately to vaporization of tissue [43]. The term is an acronym for Light Amplification by Stimulated Emission of Radiation. At shorter wavelengths, the beam coagulates vascular structures and prevents bleeding. At longer wavelengths, the energy delivered can be used to

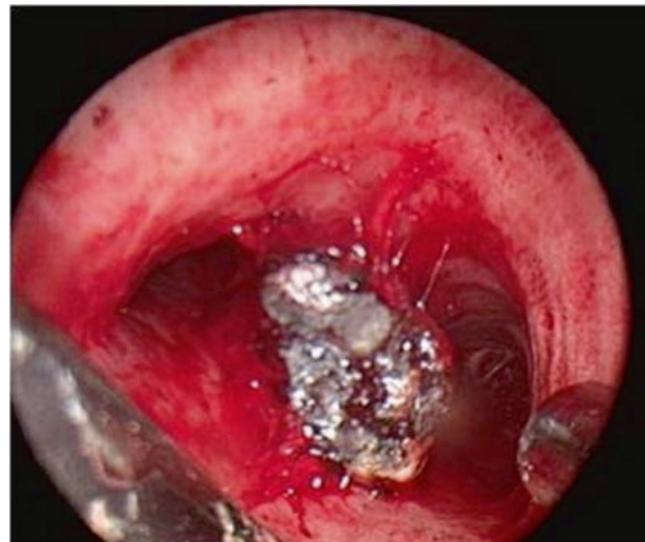


FIG. 11.5. Example of tumor debulking (image courtesy of Dr. Tawimas Shaipanich BC Cancer Agency).

resect tissue as it induces vaporization. The application of laser can be accomplished by contact or noncontact probes (usually <1 cm). There are a variety of lasers available, however for medical purposes the Nd:YAG (neodymium:yttrium aluminum garnet, wavelength 1,064 nm) and CO_2 (wavelength 10 μm) types are most widely used [44]. The former is preferred by bronchoscopists as it offers a better coagulation profile and can be used through either a flexible or rigid bronchoscope, though incisions are less precise. CO_2 laser equipment is cumbersome and its articulated arm cannot deliver the beam around corners, beyond the trachea. As such, its use is better suited for otolaryngologists working above the carina and around the larynx.

Surgical laser can be applied by interventionalists through flexible or rigid bronchoscopes. Experienced practitioners prefer rigid bronchoscopy because of the improved airway access and control [45]. In addition to isolated laser vaporization of the tumor, an alternate strategy is to devascularize and core out

the bulk of the mass in combination with physical resection using forceps or a scalpel [46]. Beyond the general anesthetic considerations of bronchoscopy, the use of laser confers the rare but catastrophic risk of airway fire. For this reason, it is prudent to minimize the inspired oxygen concentration (<40% FiO₂) as tolerated. Should an endotracheal tube be required during fiberoptic laser use, specialized tubes and/or reflective wrap may be utilized to minimize the risk of plastic combustion with the CO₂ laser [47]. However, no material used in an airway device, except metal, is completely safe from combustion if struck by a Nd:YAG laser.

Overall, complication rates are low with laser (~1%) [48] and include the aforementioned risk of endobronchial burns, hemorrhage, airway perforation, hypoxemia, arrhythmia, and even stroke. The remote possibility of cerebral air embolism is caused by the use of air for coaxial cooling of the laser and is greatly reduced by substituting CO₂ for this purpose [49]. Extra care must be taken when using laser on highly vascular posterior structures for this reason. Also, laser light can lead to retinal damage in the case of inadvertent exposure; protective eyewear is recommended for all operating room occupants. Similarly, smoke evacuation systems have been advocated in response to reports that viral particles are present in laser plume [50]. In fact, transmission of HPV to physicians during laser vaporization of papillomas has been documented [51], though others have shown that HIV particles isolated from laser exhaust are not viable in vitro [52].

Endobronchial Electrosurgery

Endobronchial electrosurgery (EBES) refers to therapeutic interventions using the direct application of electric current to tissue in a patient who is electrically grounded with an adhesive grounding pad. The delivery of thermal energy by this method will either induce coagulation or incision ("cut") depending on the precise levels of amperage and voltage [53]. Practitioners can blend these two parameters to induce the type of tissue changes they are seeking (e.g., arrest of bleeding or resection of tissue). Using a wire loop, pedunculated lesions can be cleanly excised by circumferential cutting of the supporting stalk, while sessile lesions can be debulked with dissecting probes. Essentially, the technology can be employed in virtually the same scenarios as those where laser is applied [54]. The main difference between the two is that EBES is much less expensive, requires less sophisticated equipment and technical expertise to perform [55]. Complications are also largely the same as those for laser with a significant risk of airway fire during cauterization of tissue. Electromagnetic interference during EBES may lead to malfunction of implanted electrical devices including pacemakers and AICDs [56].

Argon Plasma Cautery

Argon plasma cautery (APC) also uses electrical current to induce thermal destruction of endobronchial tissues for resection and coagulation. However, rather than using direct contact

with an electrically grounded patient to conduct current, ionized argon gas released from the tip of the probe acts as the conductor allowing for a noncontact technique [57]. The nature of the gas flow allows for energy to be directed in multiple planes from the probe tip and for targeting lesions that would otherwise be inaccessible by other modalities [58].

The depth of penetration using APC is less than that of laser or EBES, so it is most useful for superficial lesions (e.g., hemorrhagic foci) and may be used more safely near endobronchial stents [59]. Along with the usual complications of interventional bronchoscopy, APC confers both the risk of electromagnetic interference and air embolus (thought to be related to entrainment of argon gas) [60].

Balloon Bronchoplasty

Balloon bronchoplasty involves navigating a silicone balloon into a stenotic region using fiberoptic bronchoscopy alone or in combination with fluoroscopy then applying incremental, pressurized inflation. Oftentimes the airway patency achieved with isolated balloon bronchoplasty is not sustained and either demands repeated attempts or combined intervention (e.g., stenting). Malignant strictures are at notable risk for rapid re-stenosis. Although mucosal damage associated with balloon bronchoplasty is limited when compared with laser photoresection or bougie dilation, airway rupture and hemorrhage remain a risk. Other reported complications with this technique include bronchospasm, tracheitis, fever, atelectasis, and pneumomediastinum [61].

Delayed Resection Techniques

A major advantage of laser, EBES, APC, and balloon bronchoplasty is the immediate effective relief of airway obstruction and return of airway patency. There are a number of other techniques (Table 11.5) whose mode of action is delayed including photodynamic therapy, cryotherapy, and brachytherapy (Fig. 11.6). They are most often employed for nonsurgical candidates with nonobstructing lesions, for palliation of advanced malignancy, and potential cure of early staged cancer, such as carcinoma in situ [62]. They can all be performed via fiberoptic bronchoscopy and therefore rarely require the service of an anesthesiologist. Acute decompensation due to procedural complications with these techniques is less frequent than with the more invasive techniques described above.

Foreign Body Extraction and Emerging Techniques

In the absence of history, the diagnosis of foreign body aspiration may be allusive. The classic "penetration syndrome" of choke, cough, and wheeze is present only in a fraction of patients. Patients at extremes of ages are at greatest risk for aspiration owing to immature or blunted airway and swallowing reflexes [93]. In adults, the foreign body tends to impact in the distal airway, whereas in children, the material often settles in the mainstem bronchi (R>L).

TABLE 11.5. Nonoperative tumor resection techniques.

Modality	Description	Complications
Photodynamic therapy	Injection of photo-sensitive agent (dihemato-porphyrin ester) which is activated by direct exposure to light	Prolonged susceptibility to burn from sunlight Requires bronchial lavage due to pronounced tissue sloughing
Cryotherapy	Tissue destruction by rapid freezing using decompressed gas	Requires bronchial lavage due to pronounced tissue sloughing Transient fever
Brachytherapy	Radioactive beads (iridium 192) placed directly in tumor	Hemorrhage Fistula formation Bronchial stenosis Radiation exposure

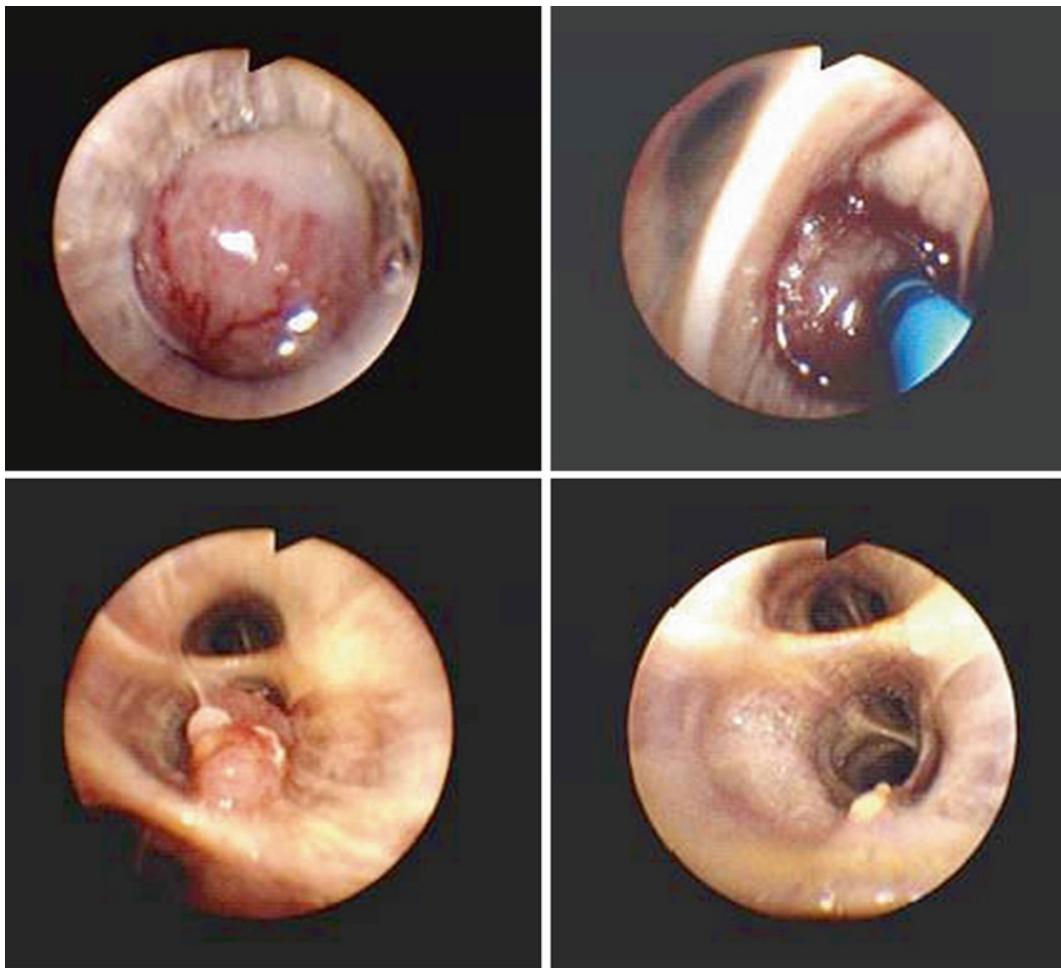


FIG. 11.6. Series depicts tumor regression in response to bronchoscopic brachytherapy (images courtesy Dr. Annette McWilliams BC Cancer Agency).

The host response and complications of foreign body aspiration are primarily dependent upon the physical properties of the aspirated object (organic vs. inorganic; sharp vs. dull), location, and duration of involvement. Organic material elicits a robust local inflammatory response culminating in tissue granulation. Prolonged impaction may cause atelectasis, postobstructive pneumonia, bronchiectasis, and bronchial stenosis. Perforation or erosion of the airway may be associated with pneumothorax, pneumomediastinum, or hemoptysis [93].

Traditionally, the rigid bronchoscope has been the instrument of choice for foreign body extraction. Contemporary strategies for managing foreign body aspiration in adults primarily employ flexible bronchoscopy [94]. Diagnostic imaging (e.g., CXR and CT scan) has a limited role in evaluating foreign body aspiration; flexible bronchoscopy remains the gold standard for diagnosis. Further, the armamentarium of devices deployed through the working channel of a flexible bronchoscope typically obviates the need for rigid bronchoscopy. These tools include a selection

of grasping forceps, balloon catheters, baskets, snares, magnets as well as laser and cryotherapy probes.

Extraction in adults is often performed with airway topicalization, light sedation, and spontaneous ventilation. If clinical status permits, an appropriate period of fasting should be respected to minimize the risk of aspiration. Tracheal intubation and mechanical ventilation may be required in the subset of patients with respiratory distress preoperatively or in those at high risk of aspiration. In either case, experts advocate strategies to avoid distal dislodgement of the foreign body during the procedure. Assuming a low risk of airway perforation or laceration, this typically will involve placement of a balloon catheter beyond the object and pulling it proximal to the tracheal carina. Once in the trachea, the foreign body can then be secured with a grasping device that is then removed from the patient's airway in tandem with the bronchoscope. For ventilated patients, temporary tracheal extubation during the final stage of removal may avoid the need to navigate the object through an endotracheal tube and the attendant risk of dislodgement or airway obstruction.

Pediatric foreign body removal is typically performed in the operating room under general anesthesia with rigid bronchoscopy. Owing to the reduced airway diameter, there is a greater perceived risk of obstruction and asphyxiation as well as air trapping from a ball valve mechanism. Gas exchange is supported with either spontaneous ventilation or intermittent positive pressure ventilation. Theoretical advantages of a

spontaneous breathing technique include fewer interruptions to ventilation, as well as a reduced risk of distal dislodgement and dynamic hyperinflation. Advocates of positive pressure ventilation cite a quite operative field as advantageous. Evidence supporting the superiority of either technique is lacking [95].

Endobronchial Valves

Newly defined roles for interventional bronchoscopists continue to emerge. Specifically, innovative interventional techniques are evolving in the management of severe emphysema and asthma. Unlike interventional strategies designed to relieve acute central airway obstruction, the role of bronchoscopy in these areas is suited for evaluation in well-designed clinical trials.

Lung volume reduction surgery (LVRS) improves pulmonary function, exercise capacity, and quality of life in selected patients at the expense of high perioperative morbidity [63]. Patients with a heterogeneous pattern of emphysema most predictably benefit from LVRS. Bronchoscopic lung volume reduction surgery (bLVRS) arose in response to the excessive morbidity associated with LVRS (see Chap. 36) and may target a wider population to include those with homogenous emphysema.

Bronchoscopic management of severe heterogeneous emphysema involves insertion of one-way endobronchial valves (Fig. 11.7) in segmental or subsegmental bronchi thereby restricting flow during inspiration and allowing

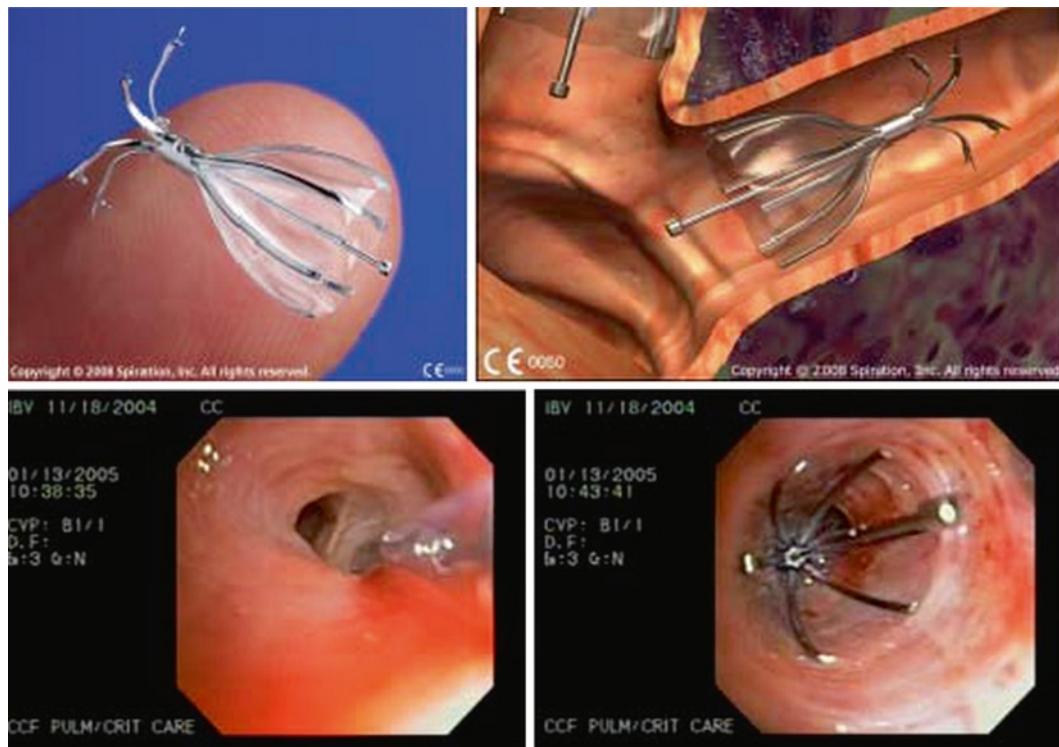


FIG. 11.7. (a, b) Spiration endobronchial valve and schematic representation of device deployment. (c, d) Endobronchial valve delivery system and insertion of valve in vitro (images a and b – courtesy of Dr S. Springmeyer, Spiration) (images c and b – courtesy of Dr. Tawimas Shaipanich BC Cancer Agency).

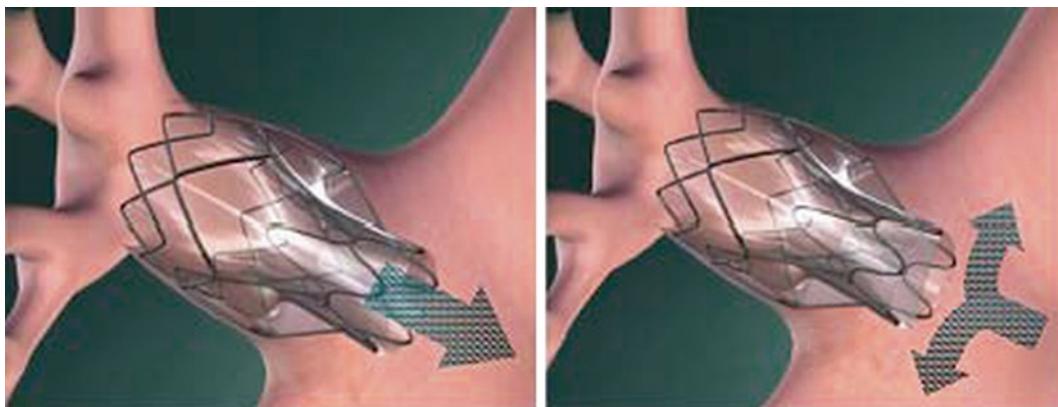


FIG. 11.8. Endobronchial valve mechanism of action: passive expiratory flow and restriction of inspiratory flow (image courtesy of Pulmonox).

passive exhalation and secretion clearance. Ultimately, the physiologic intent is to minimize dynamic hyperinflation through atelectasis (Fig. 11.8). Although completion of a multicenter randomized controlled trial evaluating bLVRS is pending (VENT), the early experience with endobronchial valve insertion described so far has been informative. Radiographic documentation of atelectasis in targeted lung segments is infrequently achieved, though clinical improvement often persists [64]. Distal collateral ventilation is cited as the mechanism for failure to achieve the intended atelectasis. Improvement in cardiac function, diaphragm and inspiratory muscle performance as well as recruitment of compressed alveoli may account for the clinical response [64].

Insertion may be performed under local or general anesthesia using flexible bronchoscopy. Relatively common complications include bronchospasm, COPD exacerbation, and pneumothorax (~10%). Valve migration and obstructing pneumonia is less frequent (~5%); fortunately, device extraction is easily performed [63]. Interestingly, compassionate use of endobronchial valves has aided in the successful management of persistent postoperative air leaks (Fig. 11.9) [65]. In all likelihood this will materialize as a new indication for device insertion.

bLVRS may also benefit patients with homogenous emphysema where hyperinflation occurs from closure of small airways. An airway bypass system that establishes a shunt between a central airway and targeted region of hyperinflated lung theoretically allows for more efficient lung emptying. This technique involves endobronchial ultrasound for vascular mapping, followed by targeted radiofrequency ablation and drug eluting stent insertion [66]. Clinical data for this procedure are limited.

Bronchial Thermoplasty

Difficult to control asthma has also received attention from bronchoscopists. Bronchial thermoplasty is a technique of applying radiofrequency energy to the airway wall, generating a tissue temperature of ~65°C. This thermal injury reduces smooth



FIG. 11.9. Endobronchial valve placement was considered in this young patient with a massive air leak associated with tumor necrosis following induction chemotherapy for lymphoma.

muscle mass but avoids tissue destruction and scarring [67]. Reduction in smooth muscle mass should theoretically improve airflow in asthmatics with airway hyperresponsiveness [68].

Diagnostic Bronchoscopy

Diagnostic bronchoscopy is almost exclusively practiced in nonoperative settings, using a flexible bronchoscope with topicalized local anesthesia and intravenous sedation. The presence of an anesthesiologist is generally reserved for patients who have tenuous cardiopulmonary reserve, impending airway compromise or for procedures which are likely to require rigid bronchoscopy or immediately before or after other thoracic surgical

procedures. Flexible bronchoscopy can be supplemented by a variety of modalities to aid in the diagnosis and staging of lung cancer, as well as a host of other pulmonary diseases. Aside from endobronchial assessment of the large airways via direct visualization, the addition of bronchial brushing, lavage and sampling expands the diagnostic yield significantly [69]. Sampling submucosal and peribronchial lesions, which cannot be directly visualized, is aided with CT, fluoroscopy or ultrasound imaging to improve diagnostic yield and limit complications. Complications attributable to these procedures are reported as less than 0.3% and include hypoxemia and cardiac arrhythmias, which are generally transient and rarely life-threatening [70].

Noninvasive Techniques

Bronchial washing involves the use of small amounts (10–15 mL) of fluid instilled in the bronchial tree to be suctioned through the bronchoscope and then sent for culture, stain, and cytology. Bronchoalveolar lavage (BAL) is the same process using larger volumes of fluid (100–200 mL) which may have greater sensitivity for the diagnosis of *pneumocystis jirovecii* (formerly *carinii*), legionella, tuberculosis and respiratory viruses such as influenza and respiratory syncytial virus. Additionally, BAL may establish a diagnosis for other noninfectious pulmonary pathologies including malignancies, alveolar proteinosis (where it can also be used therapeutically) and histiocytosis, for example [71].

Complications encountered during these procedures are generally the same as those for fiberoptic bronchoscopy, though hypoxemia may be more profound depending on the amount of fluid administered and the number of lung segments involved [72]. It seems that temperature of the lavage fluid can also have an impact on respiratory mechanics – room temperature fluids have been shown to lead to impaired TLC, FEF 25–75, and increased RV [73]. These changes do not occur with fluids at body temperature. Lavage can precipitate bronchospasm in patients with reactive airways and thus pretreatment with B-agonists and steroids, as well as the use of warmed fluid, has been advocated [74]. The release of cytokines resulting from inflamed tissues may lead to transient fevers and chills. Hemorrhage is rare and

self-limiting, occurring mainly in patients with bleeding dyscrasias or uremia. Alveolar infiltrates may remain present on chest X-ray for up to 24 h [75].

Invasive Techniques

Bronchoscopic lung biopsy (BLB) and transbronchial needle aspiration (TBNA) are nonsurgical approaches for the procurement of tissue samples required for diagnosing and staging lung pathology. The main issue with these techniques is the difficulty in delineating the location of pathologic tissue and avoiding important intrathoracic and mediastinal structures. This is problematic for two reasons: firstly, diagnostic yields are low using a blind technique and secondly, the opportunity for iatrogenic misadventure resulting in hemorrhage or air leak is heightened. The use of high-resolution CT and real-time fluoroscopy goes a long way to resolving these issues; however, these strategies are cumbersome and require a higher level of technical skill and resources. Due to the increased risk of serious complications, these approaches have fallen out of favor with many bronchoscopists and surgeons [76].

In recent years, the advent of endobronchial ultrasound (EBUS) has led to a resurgence in the interest in transbronchial tissue sampling [77]. EBUS uses a small radial or convex ultrasound probe on the end of a regular fiberoptic bronchoscope, which can be used to scan the endobronchial and peribronchial tissues of the lungs in order to directly pinpoint the structures being sought (and those sought to avoid). In particular, the use of doppler sampling allows for easy identification of vascular structures (Fig. 11.10).

Accurate sampling with EBUS is cited to exceed 90% [78, 79]. The same technology has been applied to esophagoscopy (EUS); the combination of the two approaches allows for a complete assessment of the mediastinum including all nodes accessible via traditional mediastinoscopy [80]. Both EBUS and EUS can be done under local anesthetic with sedation; however, in some centers they are conducted in the operating room under general anesthesia in conjunction with other surgical procedures.

Serious complications associated with endobronchial tissue sampling result primarily from bleeding or pneumothorax



[81]. Rarer issues include transient fever, purulent pericarditis, or hemomediastinum [82]. Overall, complication rates for BLB are the highest among these techniques with as many as 3% of cases reported to have an adverse event of some kind, and associated mortality of up to 0.1% [83]. Contraindications to BLB include coagulopathy, extensive bullous disease, vascular malformations, severe asthma, uncontrollable cough, or inability to cooperate during the procedure. Work-up should include an assessment of coagulation profile, including platelet count and kidney function. Pretreatment may include the use of DDAVP, cough-suppressant, and bronchodilators. Cessation of antiplatelet agents for 5–7 days before the procedure reduces the incidence of bleeding significantly [84].

Mechanical ventilation is not a contraindication to BLB, however, the risk of pneumothorax is three times higher in this population than in spontaneously breathing patients [85]. Reduction of PEEP below 5 cmH₂O, adequate sedation, and prophylactic neuromuscular blockade may reduce the risk of barotrauma. In anticipation of potential cardiopulmonary collapse due to tension pneumothorax, the availability of thoracostomy tube and personnel facile in rapid insertion are recommended [86].

Airway bleeding can usually be efficiently handled by the interventionalist using equipment available in the bronchoscopy suite. Standard techniques include wedging the bronchoscope into the involved segment to tamponade bleeding, or instilling 10–15 mL of iced saline (with or without epinephrine) to induce vasoconstriction [69]. Should bleeding prove more severe and unresponsive to these simple interventions, isolation of the affected lung with either a double lumen endobronchial tube or bronchial blocker may be required to prevent widespread aspiration of blood. Ultimately, urgent embolization of bronchial arteries or even surgical resection may be necessary in severe cases.

Awake Fiberoptic Intubation

Fiberoptic bronchoscopy is often employed by anesthesiologists to facilitate safe tracheal intubation in situations where conventional laryngoscopy is difficult or contraindicated. Difficult laryngoscopy may be encountered in patients with distorted anatomy or limited neck or soft tissue mobility that impedes the direct visualization of the larynx. Mask ventilation may also be a challenge in these patients, culminating in a potentially catastrophic “can’t intubate, can’t ventilate” scenario if spontaneous ventilation is compromised. Relative contraindications to direct laryngoscopy include situations where manipulation of the cervical spine may be harmful, as with ligamentous instability or unstable fractures.

The advantage of a fiberoptic bronchoscopic intubation (FOBI) is that excessive movement of the patient’s neck or mouth is not required to enable visualization of the upper airway and trachea. The bronchoscope can be guided through relatively small openings (either orally or nasally) and its maneuverability allows the operator to achieve excellent visualization without necessitating the same anatomic alignment required with direct

laryngoscopy. Once the bronchoscope has been positioned beyond the vocal cords into the trachea, it can serve as a guide over which an endotracheal tube can be passed. Some advocate approaching FOBI through the nose, as the natural curvature of the nasopharynx often results in the bronchoscope being aligned directly at the laryngeal inlet. However, nasal intubation may be less tolerated by patients, demands the use of a smaller tube and can precipitate epistaxis. The decision as to which approach is used depends on the circumstances of the individual case.

When access to the larynx is likely to be difficult, maintenance of spontaneous ventilation during intubation is the safest method of securing the airway. Often described as an awake intubation, the technique is best performed with an appropriately sedated (ideally cooperative) and reasonably comfortable patient. The type of sedation used is preferably short acting or quickly reversible, to allow for rapid return of spontaneous ventilation should the patient become apneic. Used judiciously, short-acting opioids such as fentanyl or remifentanil provide excellent sedation though they can easily lead to apnea if overdosed. Midazolam is a rapid onset intravenous benzodiazepine with amnestic properties that has a higher threshold for suppressing respiration. It should be kept in mind that the combined use of sedatives may have synergistic effects resulting in an unconscious or apneic patient at lower than anticipated doses. Reversal agents including as naloxone and flumazenil should be available in case of accidental overdose. Other adjuvant medications to consider are antisialogogues to reduce airway secretions. Anticholinergic agents used for this purpose include atropine, glycopyrrolate and scopolamine, each of which has a characteristic side-effect profile, including tachycardia (atropine>glycopyrrolate) and sedation (scopolamine>atropine) [88].

As previously described, awake patients often poorly tolerate the placement of a bronchoscope and endotracheal tube in the oropharynx and trachea. Even with effective sedation, the cough and gag reflexes are difficult to suppress and remain disruptive to the bronchoscopist. These powerful reflexes are key defenses in protecting the lungs from aspiration and are rudimentary indicators of intact brainstem function. An understanding of the basic innervation of the pharynx and larynx allows one to interrupt the afferent and efferent neural limbs to facilitate instrumentation of the airway. Basically, there are three nerves responsible for sensation in the airway: the trigeminal nerve supplies the nasopharynx, the glossopharyngeal supplies the oropharynx, and the vagus supplies the larynx and the trachea. [89]. In the upper airway, the gag response includes afferent input from the glossopharyngeal and an efferent motor arc from branches of the vagus nerve. In the lower airway, innervation above the vocal cords is primarily provided by the supralaryngeal nerve (SNL) and below the cords by the recurrent laryngeal and external SNL, all of which are vagal branches. As such the SNL controls the glottic closure reflex (which leads to laryngospasm if hyper stimulated) while the remaining vagal inputs control the cough reflex.

The application of topical anesthetic to the mucosal surfaces of the airway is the simplest way to minimize sensory stimulation and thus interrupt the afferent arm of the airway

TABLE 11.6. Topical airway anesthetic agents.

Agent	Speed of onset	Duration (min)	Maximum dose	Toxicity
Cocaine	Slow	30–60	1.5 mg/kg	Hypertension, myocardial ischemia
Lidocaine	Moderate	30–60	3 mg/kg (7 mg/kg with epinephrine)	Tinnitus, seizures, arrhythmia
Benzocaine	Fast	5–10	200 mg	Methemoglobinemia

TABLE 11.7. Airway nerve blocks.

Nerve	Approach	Considerations
Glossopharyngeal	Intra-oral: injection at base of posterior tonsilar pillar	Requires adequate mouth opening Risk of carotid injection
	Peri-styloid: injection between the mastoid process and angle of jaw	Requires palpable landmarks Risk of carotid injection
Superior laryngeal	Injection between the greater cornu of hyoid bone and superior cornu of thyroid cartilage	Requires palpable landmarks and neck extension Risk of intravascular injection
Vagus (infraglottic and upper tracheal)	Intratracheal injection through cryothyroid membrane	Requires palpable landmarks Risk of airway compromise from bleeding or trauma

reflexes before attempting an awake intubation [90]. These can be administered either by inhalation of a nebulized liquid (via facemask), direct application using an atomized spray (either blindly or through the bronchoscope itself), placement of gauze soaked in local anesthetic solution (intranasally or at the tonsilar bases) or gargling [91]. The ideal agent for topicalization is one that is quick in onset, has few side effects, with limited risk of toxicity. Absorption of these drugs through the mucous membranes of the oropharynx and lungs is unpredictable; it is possible to achieve toxic plasma levels with excessive topicalization [92]. Table 11.6 outlines the most commonly used topical agents.

Through effective topicalization, practitioners are able to achieve excellent conditions for awake intubation. Despite this, some advocate the use of nerve blocks to enhance the blunting of airway reflexes by selectively targeting the three nerves described above. These blocks are useful in clinical scenarios when local infection, blood, or secretions hinder effective topicalization. Lidocaine is usually the agent of choice for airway blocks. If nerve blocks are used in addition to topical agents, be wary of exceeding toxic levels. Obviously, these techniques involve a higher level of skill and risk the complications of intravascular injection, hematoma, and nerve injury. Further, as they require insertion of needles in the patient's neck, the performance of these blocks may themselves add to an already anxiety provoking procedure. Table 11.7 outlines the main approaches to airway nerve blocks.

Clinical Case Discussion

A 59-year-old woman presents with increasing cough, dyspnea, and oxygen requirements following a right single lung transplant for COPD (Fig. 11.11). Following a thorough clinical evaluation, a high-resolution chest CT is obtained and demonstrates a long stenotic segment distal to the bronchial anastomosis and features suggestive of an anastamotic

dehiscence. The surgeon intends to perform flexible and rigid bronchoscopy as well as balloon bronchoplasty and stenting.

Questions

Outline the anesthetic considerations for patients with previous lung transplantation

- Allograft physiology (heterogeneous compliance/impaired cough/disrupted lymphatics)
- Allograft rejection
- Vascular and bronchial anastomotic complications
- Extrapulmonary features of underlying disease requiring transplant (e.g., sarcoid)
- Septic complications of immunosuppression
- Complications/side effect of immunosuppressants

Outline the considerations of providing anesthesia for patients with a central airway obstruction

- Risk of complete airway obstruction and impossible ventilation
- Potential for dynamic hyperinflation resulting in hemodynamic compromise or barotrauma
- Considerations and complications of rigid and interventional bronchoscopy

Describe the ventilation techniques applied during rigid bronchoscopy

- Spontaneous
- Assisted
- Sanders jet ventilation
- HFJV

Describe the acute complications of balloon bronchoplasty and airway stenting

- Tracheitis
- Fever
- Atalectasis

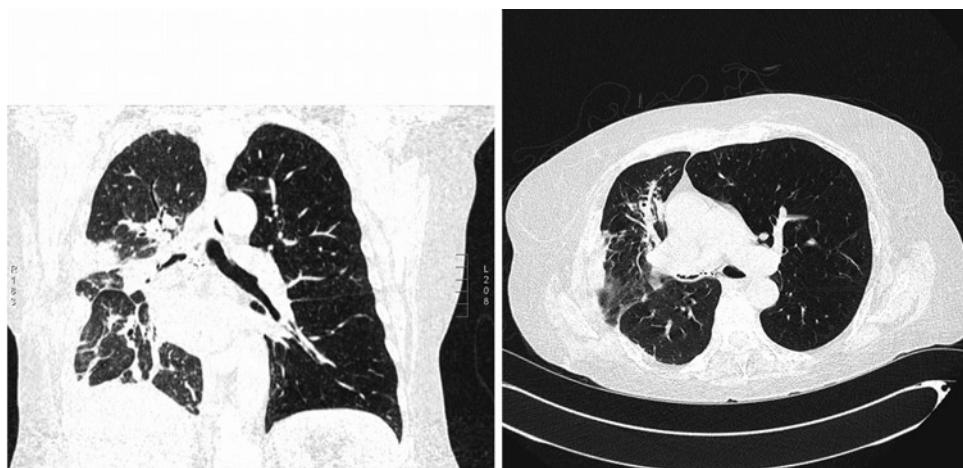


FIG. 11.11. HRCT chest demonstrating stenosis of the bronchial anastomosis following a single right lung transplant for COPD.

- Bronchospasm
- Airway disruption
- Dissemination of obstructing pneumonia
- Hemorrhage

Authors' Management

Given the heterogenous lung compliance and risk of bronchopleural fistula from anastomotic dehiscence, spontaneous ventilation was preserved in this patient. Following pre-medication with glycopyrrolate and aspiration prophylaxis, standard monitors were applied and arterial cannulation performed. General anesthesia was induced slowly by inhalation with sevoflurane. Fibreoptic inspection of the tracheobronchial tree was carried out through a laryngeal mask after thorough topicalization of the upper airway. Careful inspection of the bronchial anastomosis revealed a long stenotic segment without evidence of dehiscence. The patient was safely transitioned to positive pressure ventilation without complication. Subsequently, sevoflurane was discontinued and the anesthetic maintained with TIVA. Following balloon bronchoplasty, a rigid bronchoscope was then introduced into the airway to facilitate silicone stent insertion. Ventilation for this portion was supported with a Sanders jet injector. Given the repeated airway instrumentation during the procedure, dexamethasone was administered to mitigate glottic edema.

References

1. Limper AH, Prakash UB. Tracheobronchial foreign bodies in adults. *Ann Intern Med.* 1990;112:604–9.
2. Conacher ID, Curran E. Local anesthesia and sedation for rigid bronchoscopy for emergency relief of central airway obstruction. *Anesthesia.* 2004;59:290–2.
3. Ernst A, Simoff M, Ost M, Goldman Y, Herth FJF. Prospective risk-adjusted morbidity and mortality outcome analysis after therapeutic bronchoscopy procedures. *Chest.* 2008;134:514–9.
4. Perrin G, Colt HG, Mak MA, Dumon JF, Gorin F. Safety of interventional rigid bronchoscopy using intravenous anesthesia and spontaneous assisted ventilation. A prospective study. *Chest.* 1992;102:1526–30.
5. Metzner J, Posner KL, Domino KB. The risk and safety of anesthesia at remote locations: the US closed claims analysis. *Curr Opin Anaesthesiol.* 2009;22:502–8.
6. Folch E, Mehta AC. Airway interventions in the tracheobronchial tree. *Semin Respir Crit Care Med.* 2008;29:441–52.
7. Benumof JL. *Anesthesia for thoracic surgery.* 1st ed. Philadelphia: W.B. Saunders; 1987.
8. Pinsonneault C, Fortier J, Donati F. Tracheal resection and reconstruction. *Can J Anaesth.* 1999;46(5):439–55.
9. Mason RA, Fielder CP. The obstructed airway in head and neck surgery. *Anaesthesia.* 1999;54(7):625–8.
10. Hnatiuk OW, Corcoran PC, Sierra A. Spirometry for surgery in anterior mediastinal masses. *Chest.* 2001;120(4):1152–6.
11. Ernst A, Feller-Kopman D, Becker HD, Mehta AC. Central airway obstruction. *Am J Respir Crit Care Med.* 2004;169:1278–97.
12. Walser EM. Stent placement for tracheobronchial disease. *Eur J Radiol.* 2005;55(3):321–30.
13. Lee KS, Lunn W, Feller-Kopman D, et al. Multislice CT evaluation of airway stents. *J Thorac Imaging.* 2005;20(2):81–8.
14. Burke AJ, Vining DJ, McGuirt WF, et al. Evaluation of upper airway obstruction using virtual endoscopy. *Laryngoscope.* 2000;110(1):23–9.
15. Baroni RH, Ashiku S, Boiselle PM. Dynamic evaluation of the central airways in patients undergoing tracheoplasty for tracheomalacia. *AJR Am J Roentgenol.* 2005;184(5):1444–9.
16. Conacher ID. Anaesthesia and tracheobronchial stenting for central airway obstruction in adults. *Br J Anaesth.* 2003;90(3):367–74.
17. Wood DE. Airway stenting. *Chest Surg Clin N Am.* 2003;13(2):221–9.
18. Ho AM, Dion PW, Karmakar MK, et al. Use of heliox in critical upper airway obstruction. Physical and physiologic considerations in choosing the optimal helium:oxygen mix. *Resuscitation.* 2002;52(3):297–300.
19. Stephens K, Wood DE. Bronchoscopic management of central airway obstruction. *J Thorac Cardiovasc Surg.* 2000;119:289–96.

20. Vonk-Noordegraaf A, Postmus PE, Sutedja TG. Tracheobronchial stenting in the terminal care of cancer patients with central airways obstruction. *Chest*. 2001;120(6):1811–4.
21. Hautmann H, Gammara F, Henke M, Diehm S, Huber RM. High frequency jet ventilation in interventional fiberoptic bronchoscopy. *Anesth Analg*. 2000;90:136–40.
22. Brodsky JB. Bronchoscopic procedures for central airway obstruction. *J Cardiothorac Vasc Anesth*. 2003;17(5):638–46.
23. Smith I, Sidebotham D, McGeorge AD, Dorman EB, Wilsher ML, Kolbe J. Use of extracorporeal membrane oxygenation during resection of tracheal papillomatosis. *Anesthesiology*. 2009;110:427–9.
24. Zhou YF, Zhu SJ, Zhu SM, An XX. Anesthetic management of emergent critical tracheal stenosis. *J Zhejiang Univ Sci B*. 2007;8(7):522–5.
25. Vourch G, Fischler M, Michon F, Melchoir JC, Seigneur F. High frequency jet ventilation V manual jet ventilation during bronchoscopy in patients with tracheo-bronchial stenosis. *B J Anesth*. 1983;55(10):969–72.
26. Vaitkeviciute I, Ehrenwerth J. Con: bronchial stenting and laser airway surgery should not take place outside the operating room. *J Cardiothorac Vasc Anesth*. 2005;19(1):121–2.
27. Wahidi MM, Herth FJF, Ernst A. Interventional pulmonology. *Chest*. 2007;131:261–74.
28. Guha A, Mostafa M, Kendall JB. The Montgomery T-tube: anaesthetic problems and solutions. *Br J Anaesth*. 2001;87(5):787–90.
29. Dumon JF. A dedicated tracheobronchial stent. *Chest*. 1990;97(2):328–32.
30. Saito Y. Endobronchial stents: past, present, and future. *Semin Respir Crit Care Med*. 2004;25(4):375–80.
31. Mehta AC. AERO Self expanding hybrid stent for airway stenosis. *Expert Rev Med Devices*. 2008;5(5):553–7.
32. Finlayson GN, Brodsky JB. Anesthetic considerations for airway stenting in adult patients. *Anesthesiol Clin*. 2008;26(2):281–91.
33. Zakaluzny SA, Lane JD, Mair EA. Complications of tracheobronchial airway stents. *Otolaryngol Head Neck Surg*. 2003;128(4):478–88.
34. Bolliger CT, Sutedja TG, Strausz J, et al. Therapeutic bronchoscopy with immediate effect: laser, electrocautery, argon plasma coagulation and stents. *Eur Respir J*. 2006;27(6):1258–71.
35. Grillo HC. Stents and sense. *Ann Thorac Surg*. 2000;70(4):1142.
36. Grewe PH, Muller KM, Lindstaedt M, et al. Reaction patterns of tracheobronchial wall to implanted noncovered metal stents. *Chest*. 2005;128(2):986–90.
37. Thornton RH, Gordon RL, Kerlan RK, et al. Outcomes of tracheobronchial stent placement for benign disease. *Radiology*. 2006;240(1):273–82.
38. Ehller RL, Livingston WJ, Morgan CE. Expandable tracheal stenting for benign disease: worth the complications? *Ann Otol Rhinol Laryngol*. 2006;115(4):247–52.
39. Makris D, Marquette CH. Tracheobronchial stenting and central airway replacement. *Curr Opin Pulm Med*. 2007;13(4):278–83.
40. Urschel JD. Delayed massive hemoptysis after expandable bronchial stent placement. *J Laparoendosc Adv Surg Tech A*. 1999;9(2):155–8.
41. Hung WT, Liao SM, Su JM. Laryngeal mask airway in patients with tracheal stents who are undergoing non-airway related interventions: report of three cases. *J Clin Anesth*. 2004;16(3):214–6.
42. Davis N, Madden BP, Sheth A, et al. Airway management in patients with tracheobronchial stents. *Br J Anaesth*. 2006;96(1):132–5.
43. Simoff MJ, Sterman DH, Ernst A. Thoracic endoscopy: advances in interventional pulmonology. Malden, MA: Blackwell Futura; 2006. p. xiii, 361.
44. Van Der Spek AF, Spargo PM, Norton ML. The physics of lasers and implications for their use during airway surgery. *Br J Anaesth*. 1988;60:709–29.
45. Cortese DA. Rigid versus flexible bronchoscope in laser bronchoscopy. *J Bronchol*. 1994;1:72–5.
46. Moghissi K, Dixon K, Hudson E, Stringer M, Brown S. Endoscopic laser therapy in malignant tracheobronchial obstruction using sequential Nd YAG laser and photo-dynamic therapy. *Thorax*. 1997;52:281–3.
47. Geffen B, Shapshay SM, Bellack GS, Hobin K, Setzer SE. Flammability of endotracheal tubes during Nd-YAG laser application in the airway. *Anesthesiology*. 1986;65:511–5.
48. Wang KP, Mehta AC, Turner JF. Flexible bronchoscopy. 2nd ed. Malden, MA: Blackwell; 2004. p. xi, 287.
49. Tellides G, Ugurlu BS, Kim RW, Hammond GL. Pathogenesis of systemic air embolism during bronchoscopic Nd:YAG laser operations. *Ann Thorac Surg*. 1998;65:930–4.
50. Lobraico RV, Schifano MJ, Brader KR. A retrospective study on the hazards if the carbon dioxide laser plume. *J Laser Appl*. 1988;1:6–8.
51. Garden JM, O'Banion MK, Shelnitz LS, Pinski KS, Bakus AD, et al. Papillomavirus in the vapor of carbon dioxide laser-treated verrucae. *JAMA*. 1988;259:1199–202.
52. Baggish MS, Poiesz BJ, Joret D, Williamson P, Refai A. Presence of human immunodeficiency virus DNA in laser smoke. *Lasers Surg Med*. 1991;11:197–203.
53. Barlow DE. Endoscopic applications of electrosurgery: a review of basic principles. *Gastrointest Endoscop*. 1982;28:73–6.
54. Coulter TD, Mehta AC. The heat is on: impact of endobronchial electrosurgery on the need for Nd-YAG laser photoresection. *Chest*. 2000;118:516–21.
55. van Boxem T, Muller M, Venmans B, Postmus P, Sutedja G. Nd-YAG laser vs bronchoscopic electrocautery for palliation of symptomatic airway obstruction: a cost-effectiveness study. *Chest*. 1999;116:1108–12.
56. Ernst A, Gerard A, Silvestri GA, Johnstone D. Interventional pulmonary procedures guidelines from the American College of Chest Physicians. *Chest*. 2003;123:1693–717.
57. Grund KE, Storek D, Farin G. Endoscopic argon plasma coagulation (APC) first clinical experiences in flexible endoscopy. *Endosc Surg Allied Technol*. 1994;2:42–6.
58. Sheski FD, Mathur PN. Endobronchial electrosurgery: argon plasma coagulation and electrocautery. *Semin Respir Crit Care Med*. 2004;25:367–74.
59. Morice RC, Ece T, Ece F, Keus L. Endobronchial argon plasma coagulation for treatment of hemoptysis and neoplastic airway obstruction. *Chest*. 2001;119:781–7.
60. Reddy C, Majid A, Michaud G, Feller-Kopman D, Eberhardt R, et al. Gas embolism following bronchoscopic argon plasma coagulation: a case series. *Chest*. 2008;134:1066–9.
61. McArdle JR, Gildea TR, Mehta AC. Balloon bronchoplasty its indications, benefits and complications. *J Bronchol*. 2005;12:123–7.
62. Vergnon JM, Huber RM, Moghissi K. Place of cryotherapy, brachytherapy and photodynamic therapy in therapeutic bronchoscopy of lung cancers. *Eur Respir J*. 2006;28:200–18.
63. McKenna RJ. Endobronchial valves in the treatment of emphysema. *Semin Thorac Cardiovasc Surg*. 2008;20(4):285–9.

64. Hopkinson NS. Bronchoscopic lung volume reduction: indications, effects and prospects. *Curr Opin Pulm Med.* 2007;13:125–30.
65. Travaline JM, McKenna RJ, Giacomo TD, Venuta F, Hazelrigg SR, Boomer M, et al. Treatment of persistent pulmonary air leaks using endobronchial valves. *Chest.* 2009;136:355–60.
66. Ingenito EP, Wood DE, Utz JP. Bronchoscopic lung volume reduction in severe emphysema. *Proc Am Thorac Soc.* 2008;5:454–60.
67. Bel EH. “Hot Stuff” bronchial thermoplasty for asthma. *Am J Resp Crit Care Med.* 2006;173:941–2.
68. Cox G. New interventions in asthma including bronchial thermoplasty. *Curr Opin Pulm Med.* 2008;14:77–81.
69. Lee P, Mehta AC, Mathur PN. Management of complications from diagnostic and interventional bronchoscopy. *Respirology.* 2009;14:940–53.
70. Burns DM, Shure D, Francoz R, Kalafer M, Harrell J, et al. The physiological consequences of saline lobar lavage in healthy human adults. *Am Rev Respir Dis.* 1983;127:695–701.
71. Strumpf IJ, Feld MK, Cornelius MJ, Keogh BA, Crystal RG. Safety of fiberoptic bronchoalveolar lavage in evaluation of interstitial lung disease. *Chest.* 1981;80:268–71.
72. Pingleton SK, Harrison GF, Stechschulte DJ, Wesselius LJ, Kerby GR, et al. Effect of location, pH and temperature of instillate in bronchoalveolar lavage in normal volunteers. *Am Rev Respir Dis.* 1983;128:1035–7.
73. Wardlaw AJ, Collins JV, Kay AB. Mechanisms in asthma using the technique of bronchoalveolar lavage. *Int Arch Allergy Immunol.* 1987;82:518–25.
74. European Pneumology Task Group. Technical recommendation and guidelines for bronchoalveolar lavage. *Eur Respir J.* 1989;2:561–85.
75. Schreiber G, McCrory DC. Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. *Chest.* 2003;123:115S–28.
76. Colt HG, Prakash UBS, Offord KP. Bronchoscopy in North America: survey by the American Association for Bronchology. *J Bronchol.* 2000;7:8–25.
77. Sheski FD, Praveen NM. Endobronchial ultrasound. *Chest.* 2008;133:264–70.
78. Krasnik M, Vilmann P, Larsen SS, Jacobsen GK. Preliminary experience with a new method of endoscopic transbronchial real time ultrasound guided biopsy for diagnosis of mediastinal and hilar lesions. *Thorax.* 2003;58:1083–6.
79. Herth FJ, Lunn W, Eberhardt R, Becker HD, Ernst A. Transbronchial versus transesophageal ultrasound-guided aspiration of enlarged mediastinal lymph nodes. *Am J Respir Crit Care Med.* 2005;171:1164–7.
80. Kennedy MP, Jimenez CA, Morice RC, Eapen GA. Ultrasound-guided endobronchial, endoscopic, and transthoracic biopsy. *Semin Respir Crit Care Med.* 2008;29:453–64.
81. Kucera F, Wolfe GK, Perry ME. Hemomediastinum after transbronchial needle aspiration. *Chest.* 1990;3:466.
82. Epstein SK, Winslow CJ, Brecher SM, Faling LJ. Polymicrobial bacterial pericarditis after transbronchial needle aspiration: case report with an investigation on the risk of bacterial contamination during fiberoptic bronchoscopy. *Am Rev Respir Dis.* 1992;146:523–5.
83. Simpson FG, Arnold AG, Purvis A, Belfield PW, Muers MF, et al. Postal survey of bronchoscopic practice by physicians in the United Kingdom. *Thorax.* 1986;41:311–7.
84. Ernst A, Eberhardt R, Wahidi M, Becker HD, Herth FJ. Effect of routine clopidogrel use on bleeding complications after transbronchial biopsy in humans. *Chest.* 2006;129:734–7.
85. Papin TA, Grum CM, Weg JG. Transbronchial biopsy during mechanical ventilation. *Chest.* 1986;89:168–70.
86. O’Brien JD, Ettinger NA, Shevlin D, Kollef MH. Safety and yield of transbronchial lung biopsy in mechanically ventilated patients. *Crit Care Med.* 1997;25:440–6.
87. Slinger PD, Campos JH. Anesthesia for thoracic surgery. In Miller RD, editor. *Anesthesia Volume 2.* 7th ed. Amsterdam: Elsevier; 2009.
88. Anticholinergic drugs. In Stoelting RK, editor. *Pharmacology and physiology in anesthetic practice,* 2nd ed. Philadelphia: Lippincott; 1991. p. 244–45.
89. Simmons ST, Schleich AR. Airway regional anesthesia for awake fiberoptic intubation. *Reg Anesth Pain Med.* 2002;27(2):180–92.
90. Kunda P, Kutralam S, Ravishankar M. Local anesthesia for awake fiberoptic nasotracheal intubation. *Acta Anaesthesiol Scand.* 2000;44:511–6.
91. Mostafa SM, Murthy BVS, Hodgson CA, Beese E. Nebulized 10% lignocaine for awake fiberoptic intubation. *Anaesth Intensive Care.* 1998;26:222–3.
92. Chung DC, Mainland PA, Kong AS. Anesthesia of the airway by aspiration of lidocaine. *Can J Anaesth.* 1999;46:215–9.
93. Rafanan AL, Mehta AC. Adult airway foreign body removal. What’s new? *Clin Chest Med.* 2001;22(2):319–30.
94. Swanson KL. Airway foreign bodies. What’s new? *Semin Respir Crit Care Med.* 2004;25(4):405–11.
95. Zur KB, Litman RS. Pediatric airway foreign body retrieval: surgical and anesthetic perspectives. *Paediatr Anaesth.* 2009;19 Suppl 1:109–17.

12

Intravenous Anesthesia for Thoracic Procedures

Ron V. Purugganan

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Key Points

- Total intravenous anesthesia (TIVA) is indicated for procedures in which inhalational anesthetics may not be safely or effectively delivered, including endobronchial procedures using flexible or rigid bronchoscopy and proximal airway-disrupting surgeries. TIVA may also be beneficial in lung volume reduction surgery, lung transplantation, and thymectomy.
- TIVA is safer and more practical for thoracic procedures performed outside of the operating room, such as offsite locations, military field, or impoverished areas of the world.
- Target-controlled infusion (TCI) is a relatively new delivery system for TIVA that is based on pharmacokinetic models to optimize intravenous anesthetic delivery. TCI has many advantages over conventional calculator pumps, but is not currently available in the United States.
- Because well-established MAC-type systems for intravenous anesthetics are not available, anesthetic depth monitors are useful in monitoring patients undergoing TIVA.
- Propofol, dexmedetomidine, ketamine, and remifentanil may be used in combination with anesthetic depth monitoring to execute an effective TIVA regimen.

- This chapter reviews the balanced TIVA technique currently used at the University of Texas MD Anderson Cancer Center.

Introduction

Over the last century and a half, thoracic surgery has evolved from hurried operations with high mortality to relatively safe and controlled procedures with a good chance of survival. In early procedures, anesthetic agents and their delivery were crude, resulting in suboptimal surgical conditions in which anesthetic depth was questionable, hemodynamics were unstable, and ventilation/oxygenation subpar. The development of endotracheal intubation, lung isolation techniques, and modern anesthetic drugs was instrumental in the evolution of thoracic surgery. Modern anesthetics can reliably render a patient unconscious and immobile while maintaining hemodynamic and respiratory stability. Through these improvements of surgical conditions, more complex and time-consuming operations became possible. Furthermore, the continued evolution of intravenous anesthetic agents has made it possible for thoracic anesthesiologists to better adapt their techniques to suit specific surgical scenarios. This chapter reviews the

rationale for using intravenous anesthesia for thoracic operations, the drugs and equipment required, and the methodology involved.

Rationale for Total Intravenous Anesthesia

Traditional inhalational anesthetics have been associated (at least in animal studies) with a direct inhibition of hypoxic pulmonary vasoconstriction (HPV), the reflex arteriolar constriction that diverts blood from hypoxic segments of lung to normal areas of lung, thereby decreasing shunt fraction. In thoracic procedures, this inhibition of HPV may be detrimental to patient oxygenation levels during one-lung ventilation. In contrast, intravenous anesthetics do not appear to directly inhibit HPV, *in vitro* or in patients. Consequently, interest has focused on whether total intravenous anesthesia (TIVA) might provide better oxygenation and lesser shunt fraction than inhaled anesthetics in thoracic procedures. As little work has been done to answer this question more recently, research published in the last decade is summarized here.

Several studies have shown an advantage to using TIVA. Abe et al. studied patients receiving either isoflurane or sevoflurane followed by TIVA (propofol). PaO_2 increased significantly and shunt fraction decreased significantly after the initiation of TIVA [1]. In another study, PaO_2 was also significantly higher in patients who received TIVA for pulmonary resection than in those who received volatile anesthetics [2]. Özcan et al. compared oxygenation and shunt fraction in 100 patients undergoing one of four anesthesia techniques during one-lung ventilation: TIVA with or without thoracic epidural anesthesia (TEA) and isoflurane with or without TEA. Patient oxygenation was significantly higher and shunt was significantly lower in the two groups receiving TIVA; the addition of TEA in either study group had no significant effect [3].

Alternatively, a few studies fail to support any advantage of TIVA. Beck et al. studied 40 patients who received either propofol or sevoflurane during one-lung ventilation for thoracic surgery. They found no significant difference in shunt fraction between the two groups. Hemodynamic variables known to influence HPV (cardiac index, mixed venous oxygen tension, and arterial carbon dioxide partial pressure) were also similar between the two groups [4]. Pruszkowski et al. compared oxygenation levels in patients undergoing lung lobectomy. The patients received a thoracic epidural and either sevoflurane or propofol at levels required to maintain a bispectral index (BIS) between 40 and 60. The authors found no difference in PaO_2 levels between the sevoflurane and propofol groups. They suggest that the titration of anesthetics to appropriate BIS levels (which distinguished their study) could avoid potential negative effects of inhalational anesthetics on hemodynamics that affect shunt [5]. Lastly, Von Dossow et al. divided 50 patients undergoing pulmonary surgery into two groups – isoflurane with TEA or TIVA (propofol) – and measured shunt fraction, PaO_2 , and cardiac output. They found that the decrease in PaO_2 level

TABLE 12.1. Situations in which TIVA may be indicated.

<i>Special surgical conditions</i>
Tracheal/carinal surgery
Lung volume reduction surgery
Lung transplantation
Endobronchial procedures
Thymectomy
<i>Nonideal environments</i>
Offsite locations requiring anesthesia
Austere environments (military, developing countries, etc.)

following the conversion from two- to one-lung ventilation was less in the isoflurane group. Shunt fraction remained the same in both groups. Cardiac output was greater in the TIVA group, which may have contributed to the effect on PaO_2 [6].

Most likely, even though inhalational anesthetics suppress HPV, other factors such as surgical manipulation, cardiac output, mixed venous oxygen tension, and positive end-expiratory pressure may have a greater influence on shunt fraction than the influence of inhalational agents on HPV. Therefore, further studies are required to define the clinical significance of inhaled anesthetics on HPV in thoracic surgery.

Immunomodulatory effects of inhaled vs. TIVA techniques on the lung are another area of ongoing investigation. Animal studies have shown that propofol may have a protective effect on the lungs, especially in acute lung injury resulting from endotoxin exposure [7]. In patients undergoing cardiopulmonary bypass (CPB), propofol has been shown to regulate the pulmonary inflammatory response [8]. However, studies of thoracic surgery patients undergoing one-lung ventilation may favor the use of volatile anesthetics to decrease the inflammatory response to lung isolation [9–11]. These small studies are promising in that they show not only a significant reduction in measured inflammatory response, but also an improvement in clinical outcome. Further studies are warranted.

Although neither TIVA nor inhaled anesthetic agents provides a clear *physiologic* advantage over the other for thoracic surgery, there is solid rationale for the use of TIVA in certain circumstances (Table 12.1):

- When the delivery of inhaled anesthetics is impossible or disadvantageous, due to the nature of the operation.
- In scenarios where traditional anesthetic delivery systems may be unavailable or impractical.

TIVA in Special Thoracic Surgical Conditions

Procedures or trauma that disrupts the trachea and carina complicate the delivery of inhaled anesthesia. When the proximal airways are breached, volatile agents may escape and the quantity of anesthesia reaching the patient is uncertain. Also, the operating room is at risk of pollution from the escaped anesthetics, posing a hazard to personnel. This situation is most likely during cross-field ventilation, a technique in which the distal airways (main bronchi) are directly intubated in the surgical field to facilitate ventilation and oxygenation.

Intubation and extubation are often repeated, and airway seals are frequently compromised. In addition, certain cases may require high-frequency jet ventilation or other specialized modes of ventilation incompatible with the delivery of inhalational anesthetics [12].

Patients undergoing lung volume reduction surgery (LVRS) also benefit from a TIVA approach. Because these patients suffer from chronic obstructive pulmonary disease (COPD) and have increased dead space, end-tidal volatile anesthetic concentration is inaccurate and anesthetic levels questionable [13]. In addition, air trapping is common and the elimination of volatile anesthetic may be hindered, delaying awakening and extubation.

In the case of lung transplantation, volatile anesthetics have several drawbacks. During lung transplantation, the right ventricle is subject to increased afterload and potential failure, and the cardiodepressant effects of volatile anesthetics could be detrimental. In addition, significant intrapulmonary shunt and dead space in the transplanted lung interfere with the accuracy of end-tidal anesthetic measurements. Consequently, narcotic-based anesthetic regimens are usually administered for lung transplantation surgery. However, this is not always an ideal solution, because narcotic levels may decline unpredictably during the procedure. This decline has several possible causes: (1) narcotics may be sequestered in the CPB circuit in cases using CPB; (2) narcotics tend to accumulate in lung tissue during first pass, and a considerable amount of drug might be removed when the diseased, native lung is resected; and (3) when the donor lung is transplanted, first pass uptake is repeated and systemic narcotic levels may again drop [14]. When narcotic levels drop, more volatile anesthetics and/or narcotics must be given – but with older anesthetics, over-accumulation and delayed awakening may occur. Newer, rapidly metabolized intravenous anesthetics, on the other hand, are able to rapidly counter changes in anesthetic depth without significant risk of over-accumulation. Furthermore, in pulmonary transplant surgery requiring CPB (i.e., double-lung or heart-lung transplant), TIVA allows an uninterrupted transition to the CPB phase and back to native circulation.

Endobronchial procedures that use flexible or rigid bronchoscopy (e.g., stent placement, dilatation, biopsy, and laser procedures) also benefit from a TIVA approach. These procedures are frequently complicated by periods of apnea, the need for special ventilatory techniques such as high-frequency jet ventilation, and compromised airway seals. Thus, the delivery of volatile anesthetics may be problematical. Furthermore, these procedures frequently involve repeated alternating periods of high and low stimulation, and intravenous anesthetics can be more rapidly titrated to meet fluctuating demands. Lastly, accurate measurements of volatile anesthetics by standard mass spectrometry are hindered in procedures where helium/oxygen will be used [15].

Lastly, patients with myasthenia gravis (MG) undergoing thymectomy may benefit from a TIVA approach. MG is associated with autoimmune damage to the acetylcholine

(ACh) receptors; therefore, patients exhibit baseline muscle weakness. The thymus gland is implicated in the autoimmune response against the ACh receptors; in a select population of those with MG, symptoms improve postthymectomy. MG patients are exquisitely sensitive to neuromuscular blocking agents and volatile anesthetics, which may cause prolonged paralysis or residual muscle weakness [16]. The ideal anesthetic for such patients would avoid neuromuscular blocking agents and volatile anesthetics. Successful thymectomies have been performed without neuromuscular blocking agents using TIVA ± high thoracic epidurals. Conditions for intubation and surgery were excellent [17, 18].

Scenarios that Benefit from TIVA

TIVA is the anesthetic administration system of choice in scenarios where the logistics of having fully functional anesthesia machines may be impractical or impossible. For example, off-site anesthesia has recently become more commonplace. Many minimally invasive thoracic procedures are being carried out in nonoperating room “procedure suites.” In these circumstances, TIVA is more versatile because (1) its administration does not require a full anesthesia machine setup, and (2) it can provide different levels of anesthesia (from MAC/sedation to general).

TIVA also offers several advantages in austere environments such as battlefields, disaster zones, and developing nations. For example, volatile anesthetics are considered hazardous materials – they are difficult to store and transport, and they generate waste gases that must be properly scavenged. In contrast, TIVA agents are more easily stored, transported, and disposed. A second advantage is the reduced logistical footprint – basic TIVA equipment (infusion pump and ventilator) eliminates the traditional anesthesia machine. Additionally, TIVA equipment is more robust than traditional anesthesia machines and is more likely to perform reliably in less-than-ideal conditions. Although specialized anesthesia machines developed for military applications are available, they are more costly and complex than a simple ventilator and infusion pump setup. In fact, in its most basic form, TIVA can be administered with only a syringe and ambu-bag, which is even simpler than a basic draw-over (volatile) system. Hospitals in developed countries are routinely set up for inhalational anesthetics; thus, TIVA is usually more costly, due to the price of the agents. In developing nations, however, the cost of hardware and its maintenance usually outweighs the cost of drug, making TIVA a more economical option.

Intravenous Anesthetic Agents

Several intravenous anesthetic agents may be used in combination to execute an effective TIVA regimen. Propofol, the model drug for TIVA, and useful adjuncts for TIVA – dexmedetomidine, ketamine, and remifentanil – are reviewed below.

Propofol

Propofol remains the mainstay drug for TIVA. In addition to its favorable pharmacodynamic and pharmacokinetic profile, propofol offers distinct benefits over inhaled anesthetics. In studies comparing propofol with inhaled anesthetics in thoracic procedures, propofol reduced the postoperative decline of lung function after lung resection [19] and inhibited the catecholamine surge and adrenocorticotrophic hormone (ACTH) response during lung lobectomy [20]. Studies of propofol in nonthoracic operations have also shown advantages that may be applied to thoracic procedures; propofol reduced coughing during emergence from anesthesia [21] and the depression in bronchial mucus transport velocity associated with general anesthesia [22]. In addition, the stress hormone response [23] and the expression of proinflammatory cytokines in alveolar macrophages [24] were lower in patients receiving propofol than in those receiving inhaled anesthetics.

Dexmedetomidine

Dexmedetomidine is an alpha-2 agonist sedative–analgesic that inhibits endogenous norepinephrine release. Dexmedetomidine is eight times more selective for the alpha-2 receptor than clonidine, with an alpha-2: alpha-1 receptor ratio of 1,600:1 [25]. Evidence suggests that its main effector sites are the locus cereleus for sedative action and the spinal cord for analgesic action. Interestingly, sedation with dexmedetomidine has been observed to mimic natural sleep in that hypercapneic arousal phenomena upon exposure to a CO₂ challenge is preserved [26]. In addition to its direct sedative–analgesic properties, dexmedetomidine also reduces opioid requirements [27–34] and minimum alveolar concentration levels for inhalational anesthetics [35–37].

In thoracic surgery, dexmedetomidine may offer several physiologic benefits. It reduces perioperative oxygen consumption [38] and the sympathetic response to surgical stimulus [27, 39, 40], which may confer cardioprotective benefits. In studies of thoracic surgery patients, the use of dexmedetomidine as an adjunct to epidural analgesia reduced the need for epidural fentanyl [34] and resulted in postoperative diuresis and favorable indices of glomerular filtration, suggesting enhanced renal function [41]. In patients with pulmonary hypertension undergoing mitral valve replacement, dexmedetomidine lessened the rise in systemic and pulmonary vascular resistance poststernotomy and decreased mean arterial, mean pulmonary artery, and pulmonary capillary wedge pressures [42]. Lastly, patients recovering from thoracic surgery may benefit from the reduced occurrence of respiratory depression [43–45] and postoperative shivering [46, 47] associated with dexmedetomidine.

Remifentanil

Remifentanil is an ultra short-acting fentanyl derivative that is particularly suited to thoracic procedures. Remifentanil's rapid

onset time (1 min) and short duration of action (3–10 min) [48] are ideal for managing the fluctuating periods of high and low surgical stimulation that characterize most thoracic procedures. Because TEA is the main modality for pain relief in most thoracic surgeries, there is little need for long-acting IV narcotics that may prolong extubation and cause postoperative respiratory depression. Some situations, however, (e.g., multiple surgical sites) require supplemental longer-acting narcotics for adequate postoperative analgesia. In these cases, remifentanil may be coadministered with longer-acting narcotics to provide intraoperative analgesia for periods of high surgical stimuli without risk of over-accumulation of the accompanying narcotics.

Ketamine

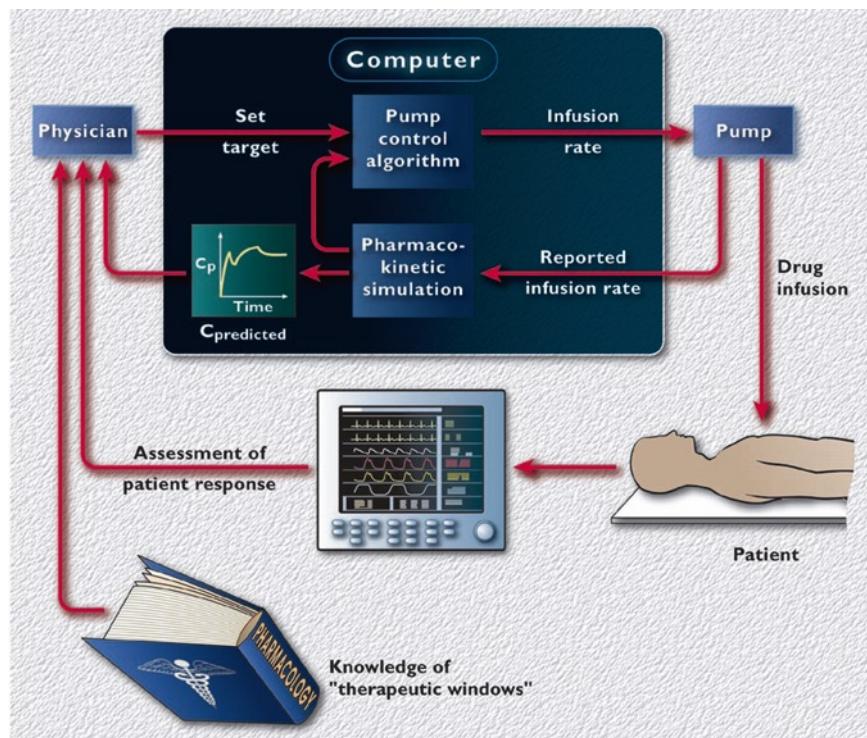
Ketamine is an *N*-methyl-D-aspartate receptor antagonist that induces a “dissociative state” in which sensory input (sight, hearing, touch) normally perceived by the patient is blocked from reaching consciousness. Because of its profound analgesic, sedative, and amnestic properties, it is occasionally used as an adjunct to propofol in TIVA regimens. Ketamine is particularly valuable for thoracic surgery because it (1) has bronchodilating properties; (2) does not depress respiration; (3) may reduce pain for up to three months postoperatively when used in conjunction with TEA for thoracotomy [49]; (4) reduces narcotic requirement; and (5) exerts sympathomimetic effects, which may be beneficial in thoracic trauma and in situations where perfusion pressure must be maintained in the presence of volume restriction.

Infusion Systems

Delivery of TIVA is more complicated than that of volatile anesthetics via the lung. While concentrations of volatile anesthetics may be approximated intraoperatively by MAC, the “MAC equivalent” for IV agents, Cp50 – the plasma concentration that will prevent a response to a given stimulus in 50% of patients – has not been fully developed for the wide range of IV anesthetics and specific clinical conditions in which they are used.

Traditionally, TIVA has been administered through calculator pumps that deliver a preset dose per unit of time. Dosages are based on recommended minimum infusion rates determined by the drug's manufacturer, and titrated to clinical effect through measurement of hemodynamics and subjective patient assessment. However, intravenous agents have a narrow therapeutic window that may be difficult to target and maintain [50]. Additionally, calculator pumps are not capable of adjusting infusion rates in response to the dynamic real-time changes in pharmacodynamics and pharmacokinetics, which can lead to under- or overdosage of the anesthetic. Therefore, computer-controlled IV drug delivery systems, or target-controlled infusion (TCI) systems, have been developed

FIG. 12.1. Delivery of intravenous anesthetic agents via target-controlled infusion (TCI). The practitioner sets a target for anesthetic concentration based on three pieces of information: knowledge of therapeutic windows for a particular drug, assessment of patient response, and predicted current concentration in the bloodstream ($C_{predicted}$). The TCI computer calculates an infusion rate based on the input target concentration and pharmacokinetic models for the drug. The pump delivers the anesthetic at the calculated rate and reports this rate back to the computer, which uses pharmacokinetic simulation to update $C_{predicted}$ (reprinted from Egan [51] with permission).



to address the shortcomings of traditional calculator pumps and mimic the convenience, advantages and familiarity of vaporizers [51].

TCI systems (Fig. 12.1) administer intravenous anesthesia based on real-time pharmacokinetic models, derived from population studies specific for each intravenous agent. These studies consider multiple factors – demographics, altered physiology, or comorbidities – that may influence drug pharmacokinetics. Appropriate administration is accomplished by incorporating a computer program coded with pharmacokinetic models of the selected agent to drive its rate of delivery – a more sensitive and accurate method of controlling concentrations than the constant rate of infusions provided by calculator pumps to achieve steady state. In other words, the practitioner focuses on target concentration, not infusion rate. The computer adjusts infusion rate constantly based on pharmacokinetic simulation of the current serum concentration of anesthetic agent in a particular patient. TCI systems reduce the subjective estimation of TIVA delivery, may deliver more consistent levels of anesthesia, and can automatically tailor the dose of anesthetic to specific phases of the surgery.

While pharmacokinetic models serve as the computational basis for TCI drug delivery, the regimen is based on the method of bolus-elimination-transfer (BET) [52, 53]. The system delivers a bolus (B) to achieve target concentration, compensates for elimination (E) by continuous infusion, and corrects for transfer (T) to peripheral tissues with an exponentially decreasing infusion. The software allows the fine-tuning of anesthetic delivery to target the steep slope of the concentration-effect curve, in which small changes in

anesthetic concentration have a relatively large effect. This tuning is accomplished through three approaches: pharmacodynamic, pharmacokinetic, and pharmaceutical [54].

The pharmacodynamic approach examines the response of the body to the anesthetic agent and adjusts delivery as needed to achieve the desired effect. This approach is usually linked with some sort of monitoring device. In contrast, the pharmacokinetic approach focuses on achieving absolute target concentrations, based on known therapeutic windows appropriate for specific anesthetic applications. Drug effect in this approach is not considered. Lastly, the pharmaceutical approach is tied to the short action (favorable pharmacokinetics) of the newer anesthetic agents. Because these agents are short-acting, it is easier to maintain a patient in the steep slope of the concentration-effect curve. If the patient is over-anesthetized, a rapid titration down of anesthetic agent results in a quick correction; if under-anesthetized, a rapid titration up is better controlled and the patient is unlikely to experience the adverse effects of “overshooting” for a prolonged period.

Because TCI systems work by *estimating* drug concentration in the bloodstream, concerns arise over the accuracy of this estimation and overall performance of TCI. Evaluation of TCI performance depends on four parameters [55]:

- Median absolute performance error (MDAPE): a measure of the accuracy of the TCI system – the median value for how close each estimate is to actual concentration.
- Median prediction error (MDPE): a measure of the direction of error of the estimates – whether the system tends to over-administer or under-administer.

- Divergence: fluctuation in the difference between estimated and actual concentrations (accuracy) over time.
- Wobble: failure to maintain a stable plasma concentration over time.

Typical MDAPE for TCI systems ranges from about 15 to 30%, while typical MDPE ranges from 3 to 20% (reviewed in [51]). MDPE has been called “clinically acceptable” in the 10–20% range [56].

Research and development for TCI currently focuses on several areas. Among the greatest of these is the fact that TCI targets plasma (not effect site) concentration. To address this discrepancy, research is focused on further modifying and refining the pharmacokinetic models to take into account effect site concentration instead of plasma concentration, and achieving effect site control via closed loop systems (e.g., anesthetic depth monitoring) [50, 57]. In the pain management of postthoracotomy patients, newly developed pharmacokinetic models for TCI patient-controlled analgesia may be an alternative to the standard method of postoperative pain management – thoracic epidural – when it is contraindicated or not feasible [58]. In fact, the greater control offered by TCI may be advantageous in these patients, who are more susceptible to the adverse effects of inadequate or excessive narcotic dosing. Another area of investigation is the use of simulation of drug delivery to compare context-sensitive half times (CSHTs) – that is, the time required to reduce by half the drug concentration after terminating an infusion at steady state [59].

Although TCI systems are widely available throughout the world, they have yet to be introduced commercially in the United States. Because TCI systems inherently fuse drug and device, the US Food and Drug Administration is uncertain whether to regulate TCI as a drug or a device and has stalled TCI system approval; this regulatory roadblock has, unfortunately, hindered commercial interest in furthering TCI technology for the US market [51].

Anesthetic Depth Monitors

Anesthetic depth monitors analyze and process a patient’s spontaneous electroencephalogram (EEG) and/or mid-latency auditory-evoked potentials (MLAEP) to gauge hypnotic depth [60]. To date, however, studies have failed to show that anesthetic depth monitors are consistently capable of either detecting intraoperative awareness or distinguishing between consciousness states [61], although anecdotal reports are encouraging. This may be of concern to anesthesia providers who consider TIVA more difficult to administer and worry that the risk of intraoperative awareness may be increased. Many of these providers are less familiar with TIVA administration than volatile anesthetic administration; for instance, they may be less familiar with the concept of C_p50 than with the analogous minimum alveolar concentration for volatile anesthetics. And even with advanced delivery systems such as TCI, direct control of effect site concentrations is currently not available.

However, an increased risk of intraoperative recall in TIVA has never been documented using the Brice interview [62] (the primary diagnostic structured interview for the assessment of intraoperative recall). Furthermore, the anesthetic depth monitor is more properly used as part of a larger overall clinical assessment scheme. Certainly, in combination with other clinical signs of inadequate hypnosis (themselves non-specific) anesthetic depth monitors may help in the titration of intravenous anesthesia. This may be particularly important for unstable patients susceptible to the cardiovascular depressant effects associated with moderate to high doses of anesthetic agents [63]. In fact, in a study on patients who underwent noncardiac surgery, mortality was correlated with cumulative deep hypnotic time as measured by BIS <45 [64].

Methodology

At the University of Texas MD Anderson Cancer Center, our TIVA technique for special thoracic procedures is a balanced technique, which allows for reduced dosages of medications. Our regimen consists of midazolam for amnesia, propofol and dexmedetomidine for hypnosis, remifentanil and TEA for analgesia, and muscle relaxants for immobilization. Anesthetic depth monitors are used routinely. Our protocol is detailed below; drug dosages are typical (and may be adjusted according to patient variability).

Premedication and Thoracic Epidural Placement

In the holding area, supplemental oxygen and IV midazolam (0.5–2 mg) are administered. Immediately prior to transport to the operating room by the anesthesia team, a dexmedetomidine infusion (0.2–0.4 μ g/kg/h) is begun. A small bolus of dexmedetomidine (0.1–0.2 μ g/kg) is administered rather than the manufacturer’s recommended bolus-loading dose (1 μ g/kg) to minimize the adverse effects associated with dexmedetomidine loading – hypo/hypertension, bradycardia, and atrial fibrillation [65]. During transport, pulse oximetry and constant communication are used to monitor the patient.

In the operating room, additional monitors (BP cuff and ECG) are applied, and the patient is positioned for thoracic epidural placement. Remifentanil infusion is begun at reduced doses (0.025–0.04 μ g/kg/min) and boluses (10–25 μ g) may be given to minimize the pain of local anesthesia infiltration and epidural placement. Upon completion of the epidural placement, anesthetic depth monitoring is initiated and a smooth transition to induction is accomplished by adding a propofol infusion (20–50 μ g/kg/min) and gradually increasing the infusions of remifentanil (to 0.05–0.1 μ g/kg/min) and dexmedetomidine (to 0.5–0.7 μ g/kg/h).

Induction

Infusions are continued through induction. Hemodynamics, anesthetic depth monitoring, and subjective assessment guide

the induction dosing of propofol (10–30 mg) and muscle relaxant to achieve adequate conditions for intubation.

Once the airway is secured, preoperative fiberoptic bronchoscopy is performed to assess airway anatomy. This potentially stimulating time for the patient may be remedied with small boluses of remifentanil (50–100 µg) and/or propofol (20–40 mg). In addition, laryngotracheal anesthesia (2% lidocaine) administered prior to bronchoscopy may lessen this response.

Invasive monitors and additional IV access may be placed pre- or postinduction as needed. A dedicated infusion line(s) ensures proper titration of IV anesthetics and prevents incompatibility issues that may arise between different medications.

Upon completion of the initial bronchoscopy, lung isolation devices are placed (if necessary) and the patient is positioned and prepped for surgery. Epidural narcotics are administered prior to skin incision, and dexmedetomidine, propofol, and remifentanil/narcotic infusions are adjusted to reflect changes in anesthetic depth monitoring and/or hemodynamics.

Maintenance

Anesthesia is maintained with propofol, dexmedetomidine, and remifentanil, titrated according to anesthetic depth monitoring and hemodynamics. Muscle relaxants are used if spontaneous ventilation is not required; they are administered by infusion to keep a train-of-four ratio of 0.4–0.5. If necessary, IV antihypertensives (rather than more anesthesia) may be used in situations where sympathetic stimulation is high, yet

a sufficient amount of anesthesia is being administered and anesthetic depth monitoring shows an adequate depth of hypnosis. Administration of local anesthesia via the epidural is usually withheld or administered in dilute concentrations to avoid sympathectomy in patients where strict volume restriction will be followed.

Emergence

In preparation for emergence, a bolus of local anesthesia followed by a constant infusion is administered via the thoracic epidural. At the start of skin closure, propofol and remifentanil are discontinued and muscle relaxant reversal is administered. The patient is maintained on dexmedetomidine (0.1–0.2 µg/kg/h) until extubation in order to impart the cardioprotective benefits of alpha-2 agonism: stable hemodynamics and rapid awakening/extubation.

Clinical Case Discussion

Case: A 52-year-old male smoker diagnosed with advanced pulmonary squamous cell carcinoma (stage IV) presents with progressive shortness of breath and orthopnea. Bronchoscopy reveals a distal tracheal mass causing moderate-to-severe airway obstruction (Fig. 12.2, left). He is scheduled for rigid bronchoscopy with stent placement to lessen tracheal obstruction (Fig. 12.2, right). This procedure will be performed in the pulmonary procedure suite.



Tracheal stent placement

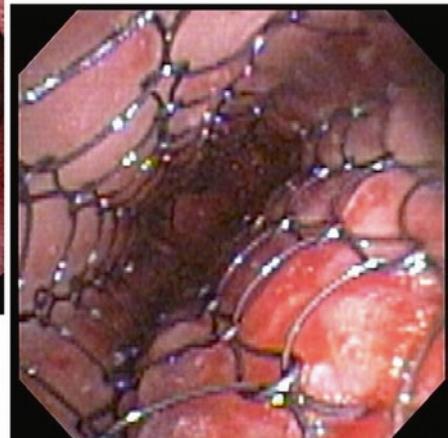


FIG. 12.2. *Left:* Rigid bronchoscopy view of an intratracheal mass obstructing the airway. *Right:* Trachea after stent placement.

Questions

- What are the disadvantages of using volatile anesthetics in this operation?
For discussion, see Sect. "TIVA in special thoracic surgical conditions" and "Scenarios that benefit from TIVA."
- What are the advantages of using (1) propofol, (2) dexmedetomidine, and (3) remifentanil in this patient?
For discussion, see Sect. "Intravenous anesthetic agents."
- What is the basic concept of target-controlled infusion, and how it is advantageous over manually controlled infusion?
For discussion, see Sect. "Infusion systems."

References

- Abe K, Shimizu T, Takashina M, Shiozaki H, Yoshiya I. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. *Anesth Analg*. 1998;87(5):1164–9.
- Pilotti L, Torresini G, Crisci R, De Sanctis A, De Sanctis C. Total intravenous anesthesia in thoracotomy with one-lung ventilation. *Minerva Anestesiol*. 1999;65(7–8):483–9.
- Ozcan PE, Senturk M, Sungur Ulke Z, et al. Effects of thoracic epidural anaesthesia on pulmonary venous admixture and oxygenation during one-lung ventilation. *Acta Anaesthesiol Scand*. 2007;51(8):1117–22.
- Beck DH, Doepfner UR, Sinemus C, Bloch A, Schenk MR, Kox WJ. Effects of sevoflurane and propofol on pulmonary shunt fraction during one-lung ventilation for thoracic surgery. *Br J Anaesth*. 2001;86(1):38–43.
- Pruszkowski O, Dalibon N, Moutafis M, et al. Effects of propofol vs sevoflurane on arterial oxygenation during one-lung ventilation. *Br J Anaesth*. 2007;98(4):539–44.
- Von Dossow V, Welte M, Zaune U, et al. Thoracic epidural anesthesia combined with general anesthesia: the preferred anesthetic technique for thoracic surgery. *Anesth Analg*. 2001;92(4):848–54.
- Votta-Velis EG, Minshall RD, Visintine DJ, Castellon M, Balyanikova IV. Propofol attenuates endotoxin-induced endothelial cell injury, angiotensin-converting enzyme shedding, and lung edema. *Anesth Analg*. 2007;105(5):1363–70. table of contents.
- An K, Shu H, Huang W, et al. Effects of propofol on pulmonary inflammatory response and dysfunction induced by cardiopulmonary bypass. *Anesthesia*. 2008;63(11):1187–92.
- Schilling T, Kozian A, Kretzschmar M, et al. Effects of propofol and desflurane anaesthesia on the alveolar inflammatory response to one-lung ventilation. *Br J Anaesth*. 2007;99(3):368–75.
- Schilling T, Kozian A, Huth C, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. *Anesth Analg*. 2005;101(4):957–65. table of contents.
- De Conno E, Steurer MP, Wittlinger M, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *Anesthesiology*. 2009;110(6):1316–26.
- Grillo HC. Development of tracheal surgery: a historical review. Part 1: techniques of tracheal surgery. *Ann Thorac Surg*. 2003;75(2):610–9.
- Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–57.
- Stoelting R. *Pharmacology and physiology in anesthetic practice*. 3rd ed. Philadelphia, PA: Lippincott-Raven; 1999.
- Sullivan EA. Anesthetic considerations for special thoracic procedures. *Thorac Surg Clin*. 2005;15(1):131–42.
- Abel M, Eisenkraft JB. Anesthetic implications of myasthenia gravis. *Mt Sinai J Med*. 2002;69(1–2):31–7.
- Bagshaw O. A combination of total intravenous anesthesia and thoracic epidural for thymectomy in juvenile myasthenia gravis. *Paediatr Anaesth*. 2007;17(4):370–4.
- Ng JM. Total intravenous anesthesia with propofol and remifentanil for video-assisted thoracoscopic thymectomy in patients with myasthenia gravis. *Anesth Analg*. 2006;103(1):256–7.
- Speicher A, Jessberger J, Braun R, Hollnberger H, Stigler F, Manz R. Postoperative pulmonary function after lung surgery. Total intravenous anesthesia with propofol in comparison to balanced anesthesia with isoflurane. *Anaesthetist*. 1995;44(4):265–73.
- Satani M, Hamada T, Nakada K, Umemoto Y, Fujii T, Takaki O. Comparison of total intravenous anesthesia and inhalation anesthesia regarding hormonal responses during lung lobectomy. *Masui*. 2005;54(10):1109–15.
- Hohlrieder M, Tiefenthaler W, Klaus H, et al. Effect of total intravenous anaesthesia and balanced anaesthesia on the frequency of coughing during emergence from the anaesthesia. *Br J Anaesth*. 2007;99:587–91.
- Ledowski T, Paech MJ, Patel B, Schug SA. Bronchial mucus transport velocity in patients receiving propofol and remifentanil versus sevoflurane and remifentanil anesthesia. *Anesth Analg*. 2006;102(5):1427–30.
- Ledowski T, Bein B, Hanns R, et al. Neuroendocrine stress response and heart rate variability: a comparison of total intravenous versus balanced anesthesia. *Anesth Analg*. 2005;101(6):1700–5.
- Kotani N, Hashimoto H, Sessler DI, et al. Expression of genes for proinflammatory cytokines in alveolar macrophages during propofol and isoflurane anesthesia. *Anesth Analg*. 1999;89(5):1250–6.
- Kamibayashi T, Maze M. Clinical uses of alpha2 -adrenergic agonists. *Anesthesiology*. 2000;93(5):1345–9.
- Hsu YW, Cortinez LI, Robertson KM, et al. Dexmedetomidine pharmacodynamics: part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. *Anesthesiology*. 2004;101(5):1066–76.
- Jalonen J, Hynynen M, Kuitunen A, et al. Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. *Anesthesiology*. 1997;86(2):331–45.
- McCutcheon CA, Orme RM, Scott DA, Davies MJ, McGlade DP. A comparison of dexmedetomidine versus conventional therapy for sedation and hemodynamic control during carotid endarterectomy performed under regional anesthesia. *Anesth Analg*. 2006;102(3):668–75.
- Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. *Anesth Analg*. 1992;75(6):940–6.
- Alhashemi JA, Kaki AM. Dexmedetomidine in combination with morphine PCA provides superior analgesia for shockwave lithotripsy. *Can J Anaesth*. 2004;51(4):342–7.
- Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia

- after major inpatient surgery. *Anesth Analg.* 2004;98(1):153–8. table of contents.
32. Sturaitis MK, Kroin JS, Swamidoss CP, Cerullo LJ, Tuman KJ. Effects of Intraoperative Dexmedetomidine Infusion on Hemodynamic Stability during Brain Tumor Resection. *Anesthesiology.* 2002;97:A310.
 33. Unlugenc H, Gunduz M, Guler T, Yagmur O, Isik G. The effect of pre-anaesthetic administration of intravenous dexmedetomidine on postoperative pain in patients receiving patient-controlled morphine. *Eur J Anaesthesiol.* 2005;22(5):386–91.
 34. Wahlander S, Frumento RJ, Wagener G, et al. A prospective, double-blind, randomized, placebo-controlled study of dexmedetomidine as an adjunct to epidural analgesia after thoracic surgery. *J Cardiothorac Vasc Anesth.* 2005;19(5):630–5.
 35. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. *Anesthesiology.* 1997;86(5):1055–60.
 36. Fragen RJ, Fitzgerald PC. Effect of dexmedetomidine on the minimum alveolar concentration (MAC) of sevoflurane in adults age 55 to 70 years. *J Clin Anesth.* 1999;11(6):466–70.
 37. Ramsay MA, Luterman DL. Dexmedetomidine as a total intravenous anesthetic agent. *Anesthesiology.* 2004;101(3):787–90.
 38. Taittonen MT, Kirvela OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state. *Br J Anaesth.* 1997;78(4):400–6.
 39. Talke P, Li J, Jain U, et al. Effects of perioperative dexmedetomidine infusion in patients undergoing vascular surgery. The Study of Perioperative Ischemia Research Group. *Anesthesiology.* 1995;82(3):620–33.
 40. Mukhtar AM, Obayah EM, Hassona AM. The use of dexmedetomidine in pediatric cardiac surgery. *Anesth Analg.* 2006;103(1): 52–6. table of contents.
 41. Frumento RJ, Logginidou HG, Wahlander S, Wagener G, Playford HR, Sladen RN. Dexmedetomidine infusion is associated with enhanced renal function after thoracic surgery. *J Clin Anesth.* 2006;18(6):422–6.
 42. But AK, Ozgul U, Erdil F, et al. The effects of pre-operative dexmedetomidine infusion on hemodynamics in patients with pulmonary hypertension undergoing mitral valve replacement surgery. *Acta Anaesthesiol Scand.* 2006;50(10):1207–12.
 43. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology.* 2003;98(2):428–36.
 44. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. *Crit Care.* 2000;4(5):302–8.
 45. Grant SA, Breslin DS, MacLeod DB, Gleason D, Martin G. Dexmedetomidine infusion for sedation during fiberoptic intubation: a report of three cases. *J Clin Anesth.* 2004;16(2):124–6.
 46. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. *Anesth Analg.* 1997;85(5):1136–42.
 47. Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C. Dexmedetomidine does not alter the sweating threshold, but comparably and linearly decreases the vasoconstriction and shivering thresholds. *Anesthesiology.* 1997;87(4):835–41.
 48. Mason P. Remifentanil. *Intensive Crit Care Nurs.* 2002;18(6): 355–7.
 49. Suzuki M, Haraguti S, Sugimoto K, Kikutani T, Shimada Y, Sakamoto A. Low-dose intravenous ketamine potentiates epidural analgesia after thoracotomy. *Anesthesiology.* 2006;105(1): 111–9.
 50. Vivian X, Leone M. Induction and maintenance of intravenous anaesthesia using target-controlled infusion systems. *Best Pract Res Clin Anaes.* 2001;15(1):19–33.
 51. Egan TD. Target-controlled drug delivery: progress toward an intravenous “vaporizer” and automated anesthetic administration. *Anesthesiology.* 2003;99(5):1214–9.
 52. Kruger-Thiemer E. Continuous intravenous infusion and multicompartment accumulation. *Eur J Pharmacol.* 1968;4(3): 317–24.
 53. Schwilden H. A general method for calculating the dosage scheme in linear pharmacokinetics. *Eur J Clin Pharmacol.* 1981;20(5):379–86.
 54. Egan TD. Advances in the clinical pharmacology of intravenous anesthetics: pharmacokinetic, pharmacodynamic, pharmaceutical, and technological considerations. *ASA Refresher Courses Anesthesiol.* 2004;32(1):71–83.
 55. Varvel JR, Donoho DL, Shafer SL. Measuring the predictive performance of computer-controlled infusion pumps. *J Pharmacokin Biopharm.* 1992;20(1):63–94.
 56. Glass PJ, Jacobs JR, Reeves JG. Intravenous drug delivery. In: Milder RD, editor. *Anesthesia.* 3rd ed. New York: Churchill Livingstone; 1990. p. 367–88.
 57. Van Poucke GE, Bravo LJ, Shafer SL. Target controlled infusions: targeting the effect site while limiting peak plasma concentration. *IEEE Trans Biomed Eng.* 2004;51(11): 1869–75.
 58. Van den Nieuwenhuyzen MC, Engbers FH, Burm AG, Vletter AA, Van Kleef JW, Bovill JG. Target-controlled infusion of alfentanil for postoperative analgesia: a feasibility study and pharmacodynamic evaluation in the early postoperative period. *Br J Anaesth.* 1997;78(1):17–23.
 59. Hughes MA, Glass PS, Jacobs JR. Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous anesthetic drugs. *Anesthesiology.* 1992;76(3):334–41.
 60. Bruhn J, Myles PS, Sneyd R, Struys MM. Depth of anaesthesia monitoring: what's available, what's validated and what's next? *Br J Anaesth.* 2006;97(1):85–94.
 61. Schneider G, Gelb AW, Schmeller B, Tschakert R, Kochs E. Detection of awareness in surgical patients with EEG-based indices—bispectral index and patient state index. *Br J Anaesth.* 2003;91(3):329–35.
 62. Nordstrom O, Engstrom AM, Persson S, Sandin R. Incidence of awareness in total i.v. anaesthesia based on propofol, alfentanil and neuromuscular blockade. *Acta Anaesthesiol Scand.* 1997;41(8):978–84.
 63. Leonard IE, Myles PS. Target-controlled intravenous anaesthesia with bispectral index monitoring for thoracotomy in a patient with severely impaired left ventricular function. *Anaesth Intensive Care.* 2000;28(3):318–21.
 64. Monk TG, Saini V, Weldon BC, Sigl JC. Anesthetic management and one-year mortality after noncardiac surgery. *Anesth Analg.* 2005;100(1):4–10.
 65. Ickeringill M, Shehabi Y, Adamson H, Ruettimann U. Dexmedetomidine infusion without loading dose in surgical patients requiring mechanical ventilation: haemodynamic effects and efficacy. *Anaesth Intensive Care.* 2004;32(6):741–5.

13

Tracheal Resection and Reconstruction

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Key Points

- The tracheal imaging (CT scan and/or MRI) must be examined by the anesthesiologist to plan the anesthetic management.
- Patients with tracheal stenosis may not become symptomatic until the tracheal diameter is narrowed to <50% of normal.
- Initial surgical management for tracheal stenosis will commonly involve rigid bronchoscopy and dilation.
- The two major methods of distal airway management for resection of tracheal stenosis are cross-field ventilation with an endotracheal tube or jet ventilation with a tracheal catheter.
- Maintenance of anesthesia during the period of tracheal resection is commonly managed with an intravenous infusion technique.

Historical Note

Surgery of the conducting airway requires diagnostic and therapeutic manipulation of the respiratory tree despite ongoing ventilation. From the very beginning of tracheal surgery, the greatest challenge facing the anesthesiologist has been how to ventilate the patient adequately before and during airway resection. Close collaboration between anesthesia and surgical colleagues was required. Early reports of tracheal tumor resection by Belsey [1] described reconstruction of the trachea after the intratracheal tube was advanced by the surgeon beyond the tracheal defect. A wire coil was constructed over the cuff of the intratracheal tube, a free graft of fascia covered the wire skeleton and the intratracheal tube was withdrawn. In 1957, Barclay reported the resection of the carina for a low tracheal tumor with deliberate endobronchial intubation of the left side by the surgeon across the surgical field [2]. The right

mainstem bronchus was sutured to the remaining trachea while the left lung was ventilated. Ventilation was then resumed via the orotracheal tube and left mainstem bronchus was sutured to the right bronchus intermedius during intermittent periods of apnea. In 1963, Grillo and Bendixen described the performance of a similar procedure under critical circumstances, in a patient whose tracheal obstruction had progressed to severe dyspnea and pulmonary hyperinflation [3]. During cross-field ventilation of the left lung, the right pulmonary artery was lightly clamped so that the unventilated lung was not perfused (Fig. 13.1). Elimination of shunt maintained “the best possible tissue oxygenation” permitting an unhurried reconstruction. “The operative requirement for complete anesthetic control during all phases of tracheal surgery is met by the technique of transitory physiologic pneumonectomy.” The same group reported the anesthetic management of 31 patients who underwent tracheal resection and reconstruction in 1969 [4]. The problems of anesthetic induction and control of the airway were fully described in this chapter first presented at the International Anesthesia Research Society in March 1969. The upper and lower airway management strategies used during a pivotal period of the development of tracheal resection and reconstruction at the Massachusetts General Hospital were elegantly presented. The discussion of the chapter at the meeting reveals the increasing appreciation of the etiology of postintubation stenoses and the clinical dilemmas that these injuries presented.

Prolonged incision and complex reconstruction of the airway in patients with compromised pulmonary function has demanded further innovation on the part of anesthesiologists and surgeons. A spectrum of ventilation strategies has been used, not only to maintain ventilation but to optimize operating conditions. Evidence of the success of this evolving collaboration lies in the large series of successful procedures reported.

Etiology of Tracheal Lesions

The trachea, carina, and major bronchi may be affected by a variety of conditions that are amenable to surgical resection and reconstruction. Airway lesions can be a result of benign or malignant etiologies (see Table 13.1), and may or may not result in significant stenosis. Congenital stenosis is typically resected during infancy, after presentation in the first few months of life. In adults, many cases of subglottic stenosis are idiopathic; frequently patients have increasing respiratory symptoms for many years, often incorrectly attributed to asthma. Postintubation injury is the most common cause of benign tracheal stenosis despite the widespread use of high-volume, low-pressure cuffs. Postintubation strictures typically show concentric narrowing whereas posttracheotomy stomal strictures tend to result in more side-to-side rather than antero-posterior narrowing. Penetrating or blunt trauma may cause life-threatening tracheal disruption, or if less severe and unrecognized, may present later as stenosis [5]. A variety of inflammatory diseases can cause airway stenosis; however, due to widespread involvement of the airway, few are considered suitable for surgical resection. Most inflammatory lesions are therefore treated with chronic tracheostomy, intermittent dilation, or stenting. A notable exception is Wegener’s granulomatosis, which can produce focal stenosis amenable to resection. Postinfectious stenotic lesions may be resected after treatment of the underlying infection. Tracheal resection is performed for primary malignancies unless metastases preclude curative

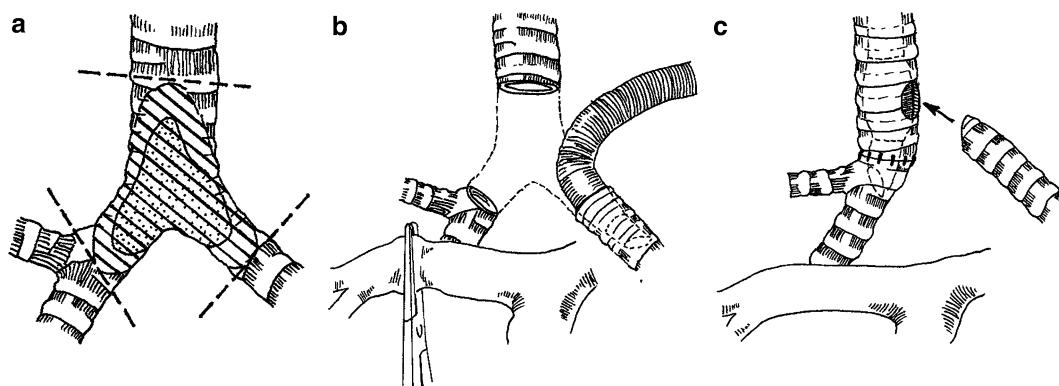


FIG. 13.1. Cross-field ventilation for carinal resection. (a) The tumor is at the carina, the patient is intubated with an orotracheal tube (not shown). (b) A sterile endobronchial tube is placed across the surgical field after the left mainstem bronchus is incised. (c) After anastomosis of the right mainstem bronchus to the remaining trachea, the cross-field endobronchial tube is removed, the orotracheal tube is advanced into a right endobronchial position, during anastomosis of the left mainstem bronchus to the trachea. Early descriptions of this technique included snaring of the right pulmonary artery during (b) to minimize shunt during one-lung ventilation (as shown here), this was later deemed unnecessary in most cases (adapted from Ref. [3]).

TABLE 13.1. Etiology of tracheal lesions amenable to resection and reconstruction.	
Benign lesions	
Congenital	
Tracheal atresia	
Congenital stenosis	
Congenital chondromalacia	
Vascular rings	
Idiopathic	
Postintubation or posttracheotomy injury	
Posterior glottic stenosis	
Subglottic stenosis (including cuff injuries)	
Tracheoinnominate artery fistula (anterior trachea)	
Tracheoesophageal fistula (posterior trachea)	
Stomal stenosis (from tracheotomy)	
Trauma	
Inflammatory	
Wegeners granulomatosis	
Postinfection (after treatment)	
Tuberculosis	
Syphilis	
Diphtheria	
Typhoid	
Malignant lesions	
Primary malignancies	
Squamous cell carcinoma	
Adenoid cystic carcinoma (cylindroma)	
Mucoepidermoid carcinoma	
Carcinoid adenoma	
Sarcoma	
Mesenchymal tumors	
Secondary malignancies	
Bronchogenic carcinoma	
Thyroid carcinoma	
Laryngeal carcinoma	
Esophageal carcinoma	

surgery, secondary neoplasms invading the trachea typically arise from the adjacent structures, and are less often amenable to surgical resection. When curative resection is not possible, many patients are treated with palliative endoscopic debridement. Similarly, endoluminal metastases which are the result of hematogenous spread from distant malignancies (including breast, colon and renal cell carcinomas, and melanoma) are typically debried or stented.

Planning Tracheal Surgery

Planning is essential in these challenging and varied procedures (see Table 13.2). A number of elements are required, starting with a clear understanding of the patient's tracheal anatomy and the resection proposed. A detailed plan for ventilation throughout induction, during the period of open airway and on emergence must be clear to the anesthesia and surgical teams. Appropriate airway equipment should be assembled and tested to ensure that it is in good working order: rigid bronchoscopes of a variety of diameters, endotracheal tubes also of a range of sizes, to be placed orotracheally or into the distal airway by the surgeon. If cross-field intubation is anticipated, sterile

TABLE 13.2. Planning for tracheal surgery.

Tracheal anatomy, resection proposed
Incision required, and patient position
Preoperative assessment
Patient monitoring
Ventilation
Transition from spontaneous to controlled ventilation
Apparatus required for ventilation
Mode of ventilation
Anesthetic drug regimen
Analgesia
Emergence, airway configuration at the end of the case

endotracheal tubes and a sterile breathing circuit are needed. Fundamental questions in planning a case include: whether there is airway stenosis, where it lies within the airway, and how small is the residual airway. Glottic and subglottic lesions almost always require dilation by the surgeon at the beginning of the procedure usually with rigid bronchoscopes of increasing diameter, although some centers use smooth round dilators. An endotracheal tube may then be placed, although often of a smaller size than would usually be used. If the lesion is in the mid-trachea or lower, and the lumen is adequate, an endotracheal tube may be placed above the lesion, without prior dilation. The anesthetic technique is influenced by the chosen mode of ventilation. Anesthetic agents with rapid onset and short duration permit a deep plane of general anesthesia with the prompt recovery and resumption of spontaneous ventilation necessary to successful extubation of patients with compromised airway anatomy. A crucial decision is: when is it appropriate to suppress the patient's spontaneous breathing and to convert to controlled ventilation techniques? In some centers it is preferred to secure the airway each time with an inhalational induction, maintenance of spontaneous ventilation, and avoidance of muscle relaxants until the initial airway is established. Most airway resections are performed in centers with experienced surgical and anesthesia teams. In many circumstances, if is suitable to induce general anesthesia with intravenous agents and give muscle relaxant prior to rigid bronchoscopy, dilation or laser resection of the airway is performed in preparation for definitive resection. This is particularly true of patients who have had a recent, uneventful rigid bronchoscopy as part of their preoperative care.

Many experienced clinical groups recommend a staged approach which starts with cautious fiberoptic bronchoscopy, after airway topicalization in the awake, spontaneously breathing patient. This permits evaluation of vocal cord function and for any malacic segments. This is often followed by rigid bronchoscopy under general anesthesia to dilate stenosis or debride obstructing tumor from the airway. The rigid bronchoscope is also the best tool to measure the position and length of the lesion in the trachea. The following measurements are made relative to the patient's upper incisors: the carina, the distal and proximal ends of the lesion, and the vocal cords. This permits an estimate of both the length of the lesion and the remaining trachea available for reconstruction. The airway can be temporarily improved by dilation in the vast majority of patients

allowing patient optimization for the definitive resection, to ensure that any bronchospasm, and pulmonary infections are treated, and for weaning of steroids if needed.

Excellent analgesia is required to optimize the chances of prompt extubation, and is planned according to the incision required by the resection. Postoperative positive-pressure ventilation is undesirable as positive pressure on a new anastomosis increases the risk of airway dehiscence.

Tracheal Anatomy and Surgical Management

The position of the lesion within the trachea will determine the site of incision and the extent of trachea requiring resection. This is often described by the number of tracheal rings removed. Using cadaver studies, Grillo investigated how much of the trachea could be removed with end-to-end reconstruction without causing undue tension or compromise of the blood supply. He determined that a median length of 4.5 cm was achievable, equivalent to seven rings [6]. The blood supply to the upper trachea is predominantly from the inferior thyroid artery, whereas the lower trachea and carina are supplied by the bronchial arteries. These studies revealed that the blood supply enters the lateral walls of the trachea in a segmental fashion; therefore the trachea is best mobilized with anterior and posterior dissection to prevent devascularization. Knowledge of the location of the tracheal lesion and the proposed extent of the airway resection are essential for planning the induction of anesthesia and the maintenance of oxygenation and ventilation. Additionally, the position of the lesion will determine the incision required and the patient position.

The Subglottis and Upper Trachea

Resection of the subglottis and upper third of the trachea may be accomplished via a collar (cervical) incision with the neck fully extended and a bolster placed behind the scapulae. The subglottic airway extends from just below the vocal cords to the lower border of the cricoid cartilage. Postintubation stenosis is the most common cause of subglottic stenosis. Complete transection of the subglottic airway will divide the recurrent laryngeal nerves, and resection is therefore modified to preserve the posterior shell of the cricoid cartilage in order to protect the entry point of these nerves. Most postintubation strictures involve relatively short segments, between 1 and 4 cm, and can be managed by segmental resection and reconstruction with a primary anastomosis. Malignancies may require more extensive resection including concomitant laryngectomy.

Prolonged translaryngeal intubation frequently results in synchronous laryngotracheal injury. The most common glottic injury is a posterior interarytenoid stenosis, which restricts vocal cord movement. These combined injuries require simultaneous high tracheal resection and laryngofissure, with

excision of the interarytenoid scar. When the subglottic anastomosis lies within a few millimeters of the vocal cords, there is significant risk of glottic edema. A Montgomery T-tube (see Fig. 13.2) is placed to support the airway and left in place several months to minimize restenosis. The T-tube is a cylindrical silicone stent with a perpendicular limb which is positioned in a small tracheostomy which makes it unlikely to become dislodged or migrate. Following laryngo-tracheoplasty the upper limb of the silicone stent lies 0.5–1.0 cm above the cords. In cases of stenotic or malacic segments of the cervical trachea without laryngeal injury, a T-tube may be left in place with the upper limb of the T-tube positioned below the cords, allowing for voice preservation.

Head flexion during primary anastomosis delivers the cervical trachea into the mediastinum to facilitate reapproximation of the edges of the trachea, and if the anastomosis appears to be at risk of being under tension, a guardian (“chin”) stitch is placed after skin closure, between the skin of the chin and the anterior chest and maintained for approximately a week (Fig. 13.2).

Mid-trachea

As with all tracheal lesions, it is important to view the imaging preoperatively in order to plan the anesthetic (see Fig. 13.3). A cervico-mediastinal incision is used for tumors of the mid-trachea and most benign lesions throughout the trachea. The upper trachea is explored through a cervical incision, which is extended via a partial sternotomy to just below the sternal angle, and separated with a pediatric chest spreader. Through this incision, the anterior carina and the right and left tracheobronchial angles can be exposed without sacrifice of the innominate vein, artery, or other great vessels. The trachea is then mobilized and incised and distal ventilation is secured. Many surgeons will request for the patient’s neck to temporarily be flexed to test the ease with which the tracheal ends will come together. The length of trachea that can be safely incised is influenced by the patient’s age, body habitus, their pathology, and prior treatment. If it is clear that the anastomosis will be under excessive tension, or a long segment of trachea requires resection, a release maneuver is performed, most often a supra-hyoid release. Muscle attachments to the superior surface of the hyoid bone and the hyoid bone itself are divided allowing the larynx to drop, adding between 1 and 2 cm of additional mobility to the trachea [7].

The resection of long segments of trachea which cannot be repaired with a primary anastomosis presents a formidable problem, and underscores the fact that the trachea is not simply a tube but is an armored structure capable of sustaining cyclical intrathoracic pressures. Historically, prosthetic grafts fail in the long term due to the formation of granulation tissue and fistulas. While devascularized aortic grafts have been used, they tend to develop malacic components. More promising reconstructive techniques such as fasciocutaneous forearm flaps stiffened with C-shaped segments of rib cartilage

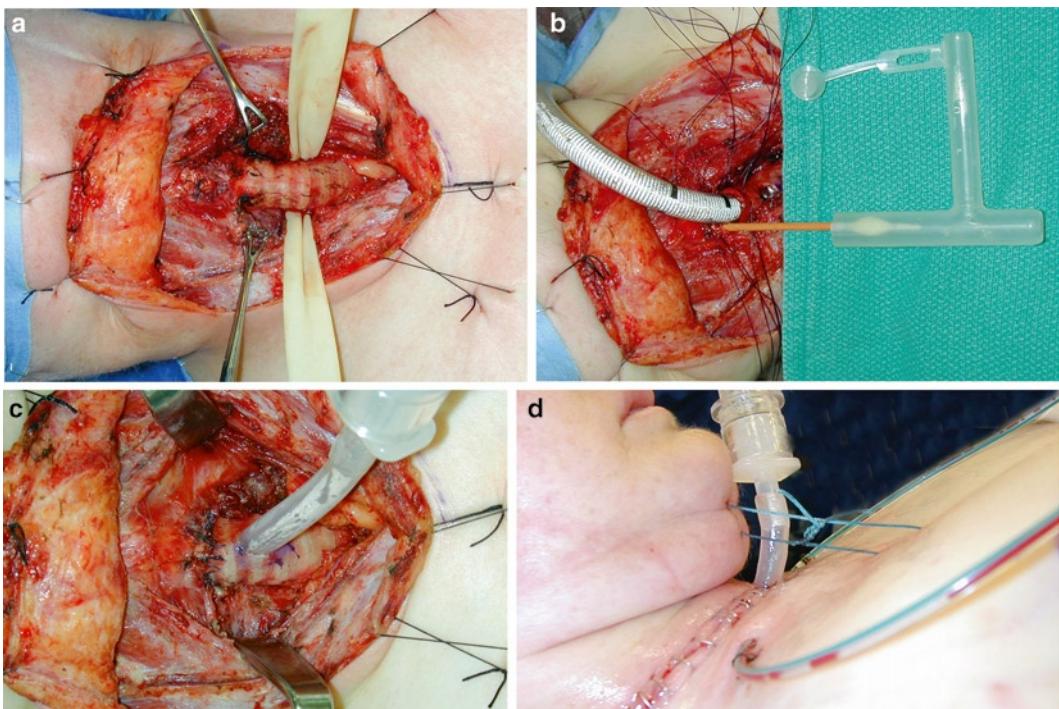


FIG. 13.2. Airway management for high tracheal resection. (a) Mobilization of the trachea, the patient's head is to the left of the photograph. (b) A sterile cross-field endotracheal tube has been placed in the distal trachea. A Montgomery T-tube will be placed, the balloon of a Fogarty catheter will be inflated to obstruct the proximal limb, to allow ventilation via the distal limb. The Fogarty catheter is passed retrograde through the patient's mouth. (c) Ventilation via the Montgomery T-tube external limb during closure of the incision. A standard endotracheal tube connector has been inserted into the external limb of the T-tube. (d) Head flexion and the guardian ("chin") stitch. The Fogarty catheter is deflated and removed when spontaneous ventilation is reestablished. The guardian stitch is removed after a week (photos courtesy of Dr. Andrew Pierre, Division of Thoracic Surgery, Department of Surgery, Toronto General Hospital).



FIG. 13.3. A three-dimensional CT reconstruction of a mid-tracheal tumor. This patient was managed with rigid bronchoscopy and debriement prior to tracheal resection.

and decellularized tracheal allograft repopulated with the recipient's own chondrocytes and airway epithelial cells have recently been used to replace the trachea [8].

Carinal Resection

The incision depends on the type of carinal resection. Carinal resection without pulmonary parenchymal resection is approached through a full sternotomy. The pericardium is opened anteriorly and the exposure is facilitated by mobilization of the aorta and both main pulmonary arteries (Fig. 13.4). Tracheal resection is usually limited to less than 4 cm at the carinal level. When there is anastomotic tension, a hilar release is performed with a U-shaped incision of the pericardium, which allows hilar structures to advance by about 2 cm. Laryngeal release is not deemed helpful for carinal resection and a chin stitch is not routinely used. Resection of the carina may be combined with a right or left pneumonectomy, or right upper lobe bronchial sleeve resection. Left carinal pneumonectomy may be performed via a sternotomy, a left postero-lateral thoractomy, or a "Clamshell" (bilateral trans-sternal thoracotomy) incision. When all or part of the right lung requires resection, a right postero-lateral approach is used. Careful patient selection and optimization is essential to the success of these technically demanding and high-risk surgeries [9].

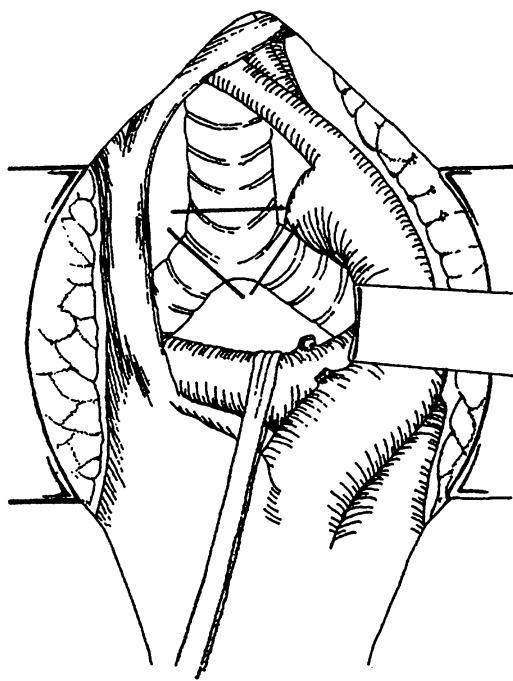


FIG. 13.4. Exposure of the carina via a sternotomy.

Patient Characteristics

Idiopathic tracheal stenosis is a diagnosis found almost exclusively in females, often presenting for resection in their fifth decade of life, many have had progressive symptoms for up to 10 years. At least one third report clinically significant reflux, and at least as many are obese which may be due to their exercise limitation. Patients with postintubation and post-tracheotomy stenoses have a mean age in their forties at the time of presentation and not infrequently have diabetes mellitus, cardiovascular disease, asthma, or chronic obstructive pulmonary disease, all conditions that may have required prior intubation. These comorbidities increase the likelihood of perioperative complications. Patients with tracheal tumors tend to be a decade older, tend less to be diabetic or obese, and are more likely to smoke, with the associated risk of vascular disease. It must be noted that some primary tracheal tumors are not associated with smoking and can present at any age [10].

Most patients are symptomatic, the most common being dyspnea on exertion, but a careful history may reveal orthopnea, a brassy cough, difficulty clearing secretions, and wheezing. Malignant tumors may produce hemoptysis. Patients should be examined for evidence of airway obstruction, the use of accessory muscles of respiration, or stridor. In adults, narrowing of the lumen to less than 50% of its normal cross-section (i.e., approximately <10 mm) results in dyspnea with significant exertion, narrowing to less than 25% of its normal cross-section will usually produce dyspnea and stridor at rest. Stridor at rest is a sign of significant airway obstruction, likely the tracheal diameter is 6 mm or less [11]. These patients are

at risk of acute airway obstruction with a mucus plug. Stridor is classically more pronounced in inspiration when stenosis is extrathoracic, if the lesion is intrathoracic the stridor may be predominantly in expiration, particularly if there is significant malacia. In addition to auscultation of the lungs and trachea, the patient's neck mobility should be evaluated.

Preoperative Assessment

The anesthesiologist should review all available information delineating the patient's airway pathology. The chest X-ray may be deceptively normal. A CT scan of the neck and thorax should be performed with thin cuts along the entire airway. Increasingly, three-dimensional images are being constructed from helical CT data. This imaging is helpful in defining the relationship of the lesion to the vocal cords and carina, and as a complement to prior endoscopy helps in planning airway management.

Pulmonary function tests, including spirometry, are usually performed unless the patient is at risk of imminent airway obstruction. Fixed airway stenoses cause limits both inspiratory and expiratory flow at similar flow rates. A variable extrathoracic airway obstruction limits inspiration much more than exhalation. Conversely, with a variable intrathoracic lesion the patient is able to inhale reasonably well, but expiratory flow limitation is produced. It should be noted that the quality of flow volume loops are very much dependant on patient effort. The characteristic findings of expiratory flow limitation may be obscured by small airways disease such as asthma or COPD [12]. The absence of classic spirometric patterns does not predict the absence of pathology and the presence of findings does not reliably indicate the degree of obstruction. Imaging of the airway is far more useful in planning surgery.

Manipulation of airway and mediastinal structures intraoperatively may provoke a significant sympatho-adrenal stress response [13]. Increases in heart rate and both systemic and pulmonary artery pressures are seen and may be prolonged. Myocardial oxygen consumption rises and dysrhythmias may occur. The incidence of myocardial ischemia in older smokers during and after rigid bronchoscopy alone may be as high as 10–15% of patients [14]. Preoperative ECG should be obtained in all patients to assess cardiac rhythm. Patients over 40 with symptoms or significant risk factors for coronary artery disease should be investigated with echocardiography, myocardial perfusion imaging, and with coronary angiography if indicated. Risk stratification is then possible, with appropriate institution of treatment. Cardiac assessment is recommended when carinal resection is required especially when combined with pneumonectomy. If significant coronary artery lesions are identified, the decision to proceed with definitive surgery rather than palliation should be decided on a case-by-case basis. Quantitative ventilation and perfusion scans may be warranted when the resection of considerable lung parenchymal is anticipated [15]. In all

patients considered for tracheal resection, the identification and treatment of reversible pulmonary disease is important. Repeated airway dilation or stenting may permit a period of medical optimization of the patient [16]. Smoking cessation is vital, particularly as patients who have undergone airway resection often struggle to mobilize secretions. Postoperative mechanical ventilation is undesirable: the presence of an endotracheal tube may predispose new suture lines to necrosis and dehiscence. Severe respiratory compromise due to parenchymal lung disease or neuromuscular disorder is a serious concern and may preclude tracheal resection [17].

Patient Monitoring

In addition to secure peripheral intravenous access and standard anesthetic monitors, an arterial catheter is placed for continuous blood pressure measurement. When an intrathoracic approach to the trachea is used, many anesthesiologists choose the left side for the radial arterial line. The innominate artery lies anterior to the trachea and compression or division of this vessel will render inaccurate arterial pressure measurement in the right arm. Arterial cannulation also provides immediate access to blood gas analysis which is essential during interrupted ventilation, during ventilation with techniques that preclude capnography, and in the event of postoperative respiratory distress. Central venous cannulation may be used if indicated by the proposed surgery (i.e., including a major pulmonary resection) and cardiopulmonary status of the patient. Avoidance of the area of incision must be considered in catheter placement; a jugular, subclavian, or antecubital approach may be used. A urinary catheter is placed, even if a simple resection is accomplished quickly, the patient's mobility is often reduced for several days due to postoperative neck flexion. The patient's temperature is monitored and normothermia should be maintained. In the rare instance of cervical exenteration, where elective division of the innominate artery is contemplated, placement of EEG monitoring has been recommended [18].

Ventilation Strategies

Surgical intervention in the airway presents unique ventilation difficulties. Clinicians have devised creative solutions for these challenges and there has been a proliferation of ventilation techniques applied to the open airway (see Table 13.3).

Distal Tracheal Intubation, Intermittent Positive Pressure Ventilation (IPPV)

Early reports of tracheal tumor resection described reconstruction of the trachea after an endotracheal tube was advanced by the surgeon beyond the tracheal defect [1]. Advancement of a full-sized orotracheal tube across the surgical field into the distal trachea or bronchus is an option currently seldom used, as the large diameter obstructs access to the surgical field. Endobronchial tubes are long single-lumen tubes of reduced diameter, with a small volume, shorter cuff positioned close to the tip. They are favored by some clinicians for certain tracheal resections. They can be positioned in the trachea beyond the lesion under bronchoscopic guidance past a mid-tracheal lesion or placed in the contralateral bronchus when a thoracotomy is required for carinal resection or carinal pneumonectomy. The endobronchial tube's slender profile allows much of the surgery to be accomplished while the tube remains within the trachea, and distal ventilation is maintained. Alternatively, these tubes can be withdrawn when the airway is opened and distal ventilation provided across the surgical field. Drawbacks of these tubes include a possible air leak that occurs when the endobronchial tube is positioned in the trachea, as the balloon has a relatively small volume.

The cuffs are prone to rupture when the tracheal is being repaired in close proximity, requiring replacement [19]. A variety of endobronchial cuffs have been described although many are no longer available [20]. In our institution, the Phycon endobronchial tube (Fuji Systems, Tokyo, Japan) is used (Fig. 13.5). The ideal endotracheal tube for tracheal reconstruction has been described as a long, flexible, reinforced tube with a short,

TABLE 13.3. Characteristics of modes of ventilation during airway surgery.

	Able to ventilate open airway	Immobility of operative field	Specialized equipment required	Airway pressure – pressure/monitoring	Potential for barotrauma	Gas entrainment	Airway gas composition
IPPV	No	No	No	Pressure is dependent on ventilator settings/reliable	Minor	No	Stable, accurate monitoring
LFJV	Yes	No	No	Intermittently high/difficult	Yes, high	Yes	Variable, difficult to monitor
HFJV	Yes	Yes	Yes	Can be high, gas trapping common/difficult, especially around jet nozzle	Yes	Yes	Variable, difficult to monitor
HFPPV	Yes	Yes	Yes	Low peak and mean transpulmonary pressure/difficult	Yes	Minor	Stable, accurate monitoring

IPPV intermediate positive pressure ventilation; LFJV low frequency jet ventilation; HFJV high-frequency jet ventilation; HFPPV high-frequency positive pressure ventilation

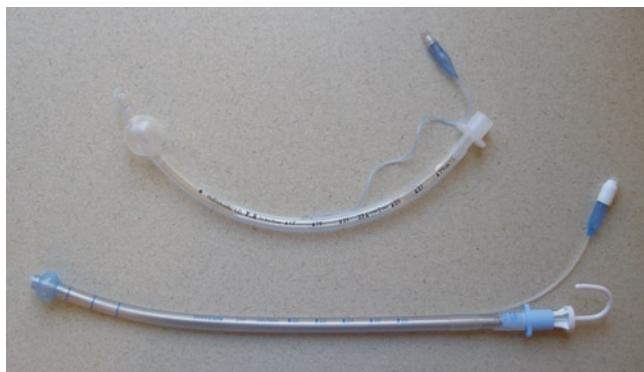


FIG. 13.5. A 7.5-mm ID Phycon endobronchial tube (*lower tube*) (Fuji Systems, Tokyo, Japan) as compared to a 7.5-mm ID standard endotracheal tube (*above*). The standard tube is 32 cm long, the armored endobronchial tube is 40 cm and is also available in 5.5 mm, 6.5 mm ID sizes. Note the small endobronchial cuff size, the lack of both bevel and Murphy eye on the distal end of the endobronchial tube.

low-pressure, high-volume cuff and a short segment beyond the cuff, to allow the ventilation of both lungs through a short tracheal stump without encroachment on the operative site, unfortunately no ideal endotracheal tube is currently manufactured [21].

The use of cross-field intubation and ventilation of the distal airway were first described for the resection of a low

tracheal tumor; the left bronchus was cannulated on the field by the surgeon, while the right mainstem bronchus was sutured to the remaining trachea. Ventilation was then resumed via the endotracheal tube and the left bronchial anastomosis was performed. Geffen described the variations of cross-field ventilation to be used for high and low tracheal lesions [4]. An orotracheal tube is placed, above the lesion. As the airway is divided, the surgeon advances a second, sterile endotracheal tube across the field into the distal trachea (Fig. 13.6). In our institution, when subglottic resection is performed, a sterile reinforced endotracheal tube is inserted in the distal trachea, and the proximal end of the tube is passed by the patient's cheek, under the sterile drapes to be connected to the anesthetic circuit. Resection of the mid or lower trachea necessitates the use of a second, sterile anesthetic circuit originating from the surgical field, passed over the drapes. Typically a relatively small endotracheal tube is placed in the distal airway to permit the placement of posterior sutures while the tube remains in the distal airway, held anterior by the surgeons. After reanastomosis of the posterior trachea, the distal tube is withdrawn and the orotracheal tube is readvanced and is used for ventilation. Lower tracheal and carinal resection requires some modification of the technique (Fig. 13.7). The distal tube is advanced into the left mainstem bronchus below the lesion. The resected

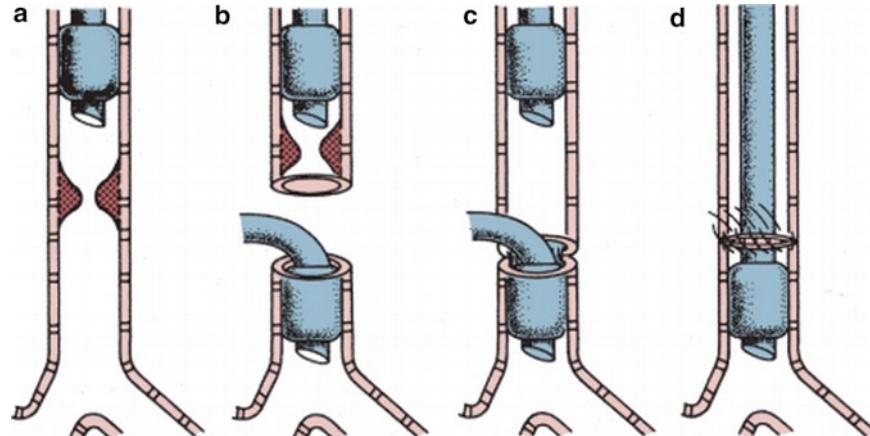


FIG. 13.6. Airway management for resection of a high tracheal lesion. (a) Orotracheal intubation above the lesion. (b) With tracheal incision, a sterile cross-field endotracheal tube is placed distal to the lesion. (c) The posterior wall of the anastomosis is sutured. (d) The cross-field endotracheal tube is removed, the orotracheal tube is advanced across the anastomosis, and the anterior anastomosis is completed (this figure was published in [75]).

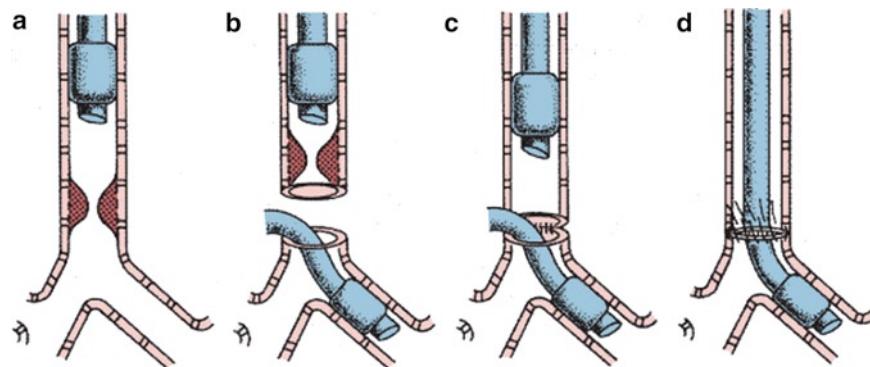


FIG. 13.7. Airway management for resection of a low tracheal lesion. (a) Orotracheal intubation above the lesion. (b) A sterile cross-field endotracheal tube is placed in the left mainstem bronchus. (c) The posterior wall of the anastomosis is sutured. (d) The cross-field endotracheal tube is removed, the orotracheal tube is advanced across the anastomosis into an endobronchial position, and the anterior anastomosis is completed (this figure was published in [75]).

trachea and the right mainstem bronchus are anastomosed, the orotracheal tube is advanced through the suture line and one-lung ventilation to the right side is accomplished while the left mainstem bronchus is anastomosed to the side of the trachea. The orotracheal tube is then withdrawn above both suture lines until extubation. This technique necessitates intermittent periods of apnea as surgeons withdraw the distal tracheal tube for better exposure and placement of sutures. Increased oxygen concentration is used when ventilating (>70%) in order to delay desaturation. Periods of moderate hypercapnia are inevitable, but are usually well tolerated. Independent distal cannulation of both bronchi has been described, and a variety of endotracheal tubes of different sizes should be available for distal cannulation [22].

Low Frequency Jet Ventilation

Jet ventilation releases high gas flow through a small orifice, permitting ventilation via laryngoscopes, bronchoscopes, and the open airway with minimal obstruction of the surgical field. Low frequency jet ventilation (LFJV) is accomplished by the release of gas under high pressure (50–60 psi) through an orifice (~1 mm) as described by Sanders [23]. A pressure regulator is required to maintain constant flow and a handheld on-off valve is released intermittently; jet pulses are delivered at a rate of 10–20/min. A distinct advantage of this approach is its simplicity and lack of specialized equipment. The use of lengthy catheters of small caliber, advanced through the orotracheal tube, permits ventilation of distal airways. Physiologic tidal volumes are generated and chest or lung movement is clearly visible.

LFJV with intermittent apnea was first described in tracheal resection in the 1970s [24, 25] and a variation of this technique is still favored by some groups [26]. The use of a narrow lengthy catheter permits ventilation of the distal airway using a device well away from the surgical field, their diameter is unlikely to obstruct surgical access to the airway. The ultimate catheter position varies with the procedure performed. A high tracheal stenosis may not admit a regular size endotracheal tube, and jet ventilation via a long small orotracheal tube has been used throughout resection [27]. More often an orotracheal tube is placed above the tracheal lesion and the narrow ventilation catheter is advanced into the distal airway after incision of the trachea. The use of independent, simultaneous catheter ventilation of each bronchus has been described in carinal resection [28]. Unpredictable tidal volumes are generated using LFJV, they are however sufficiently large to cause disruption of the surgical field and intermittent apnea is usually required. When high driving pressure (50–60 psi) is used through a narrow catheter, a high flow jet is produced (up to 100 L/min) entraining air, blood, and debris from the field into the distal airway. Blood may spray from the surgical field. When larger ventilation catheters are used, high flows can be maintained with lower driving pressure, air entrainment is reduced, permitting less dilution of

the oxygen jet as demonstrated by the high arterial oxygen tensions that can be achieved, longer periods of apnea are therefore possible [26].

High-Frequency Jet Ventilation

High-Frequency Jet Ventilation (HFJV) resembles its low frequency counterpart in that gas is delivered from a high-pressure gas source via a stiff, small bore catheter positioned in the airway. Rather than a handheld switch, the jet stream is cut by a high-frequency pneumatic or electronically controlled flow interrupter. As the high-velocity gas jet enters the airway, additional gas is entrained at the jet nozzle, contributing to the delivered tidal volumes which remain small compared to conventional ventilation [29]. Variables that can be regulated during HFJV include driving pressure, frequency, and inspiratory time, usually set at 20–30% of the cycle. Ventilation rates span 100–400 breaths/min, tidal volumes delivered are <1 mL/kg. The mechanical effects of the use of high frequencies are crucial to the understanding of gas transfer in high-frequency ventilation. Increasing the respiratory rate decreases the emptying time of the lung, moderate gas trapping occurs and the lung is held in a distended state. Peripheral airway pressures have been shown to be continuously positive using all high-frequency techniques with low mean and peak pressures maintained [30–32]. An obvious advantage when ventilating the open airway is that lower peak pressures are generated as compared to conventional ventilation optimizing lung recruitment with much less air leak. The use of low tidal volumes at high respiratory rates produces minimal movement of the operative field, and interruption of ventilation is not required during many procedures. The slender catheters used minimally obstruct the surgical field.

HFJV has been studied in experimental tracheal airway disruption; the gas driving pressure and size of the jet nozzle were shown to be crucial. When a constant driving pressure was used, increased nozzle size was required to maintain gas exchange with increasing air leak; however, a larger nozzle used with a smaller air leak resulted in lung overdistension and systemic hypotension [33]. Clinically, increased driving pressure and inspiratory time can result in impedance in expiratory gas flow, gas trapping, development of auto-PEEP, and impaired CO₂ elimination [34].

When HFJV is used in the intensive care unit, the ventilating catheter is advanced through an orotracheal tube, however the optimum position of the catheter tip is the subject of considerable debate [35]. During airway surgery, the ventilating catheter is advanced across a stenosis or surgically created defect; catheter position is therefore dictated by the nature of the procedure. The use of a HFJV via a catheter placed through a laryngeal mask airway (LMA) has been described for the resection of a high tracheal stenosis [36]. Catheters may be advanced through an orotracheal tube into the mid or distal trachea for resection of tracheal segments [37], into the distal bronchus for carinal or sleeve resection [38], and bilateral

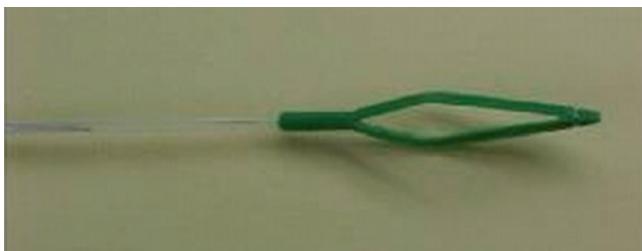


FIG. 13.8. The basket tip of the Hunsaker MonJet ventilation catheter (Xomed, Jacksonville, FL). The collapsible basket is designed to center the catheter in the airway and to reduce catheter-whip injuries to the walls of the airway during jet ventilation.

bronchial catheters have been reported in carinal resection in a patient with limited respiratory reserve, when desaturation occurred during HFJV of one lung [39]. These reports emphasize that ventilator frequency and driving pressure must be adjusted to the patient's respiratory compliance and the proportion of lung segments being ventilated at any time.

“Whip motion” of the distal catheter tip causing possible tracheal laceration and pneumothorax is a concern with all catheter ventilation techniques. The Hunsaker jet ventilation catheter (MonJet, Medtronic Xomed, Jacksonville FL) has a distal, collapsible basket-like support to maintain the catheter tip in the center of the airway and to reduce whip injuries and is used in some centers for airway resection [40] (see Fig. 13.8).

High-Frequency Positive Pressure Ventilation

High-frequency positive pressure ventilation (HFPPV) of small tidal volumes (3–5 mL/kg breaths at 60 breaths/min) may be delivered using a conventional ventilator of low internal volume and negligible internal compliance; known volumes and gas mixtures are delivered. External PEEP may be added and there is little hemodynamic derangement described. HFPPV can be applied via an insufflation catheter placed at the tip of an endotracheal tube. An injection catheter with multiple side holes is recommended to both increase turbulence thereby reducing catheter whip and to minimize gas entrainment. Eriksson et al. [41] first described tracheal resection using HFPPV with gas delivery via a rigid bronchoscopic during examination of the lesion, and via a 5 mm diameter insufflation catheter threaded into the distal trachea during resection and anastomosis. El-Baz et al. [42] described the use of HFPPV during complex tracheal reconstruction using a 2-mm insufflation catheter via a Montgomery T-tube. The same type of catheter inserted down the endotracheal tube and across the resected airway for HFPPV during sleeve resection and carinal resection was further reported [43, 44]. Excellent surgical conditions with minimal motion of the field and uninterrupted access to the circumference of the anastomosis were described, and continuous outflow of gas through the open bronchus was felt to minimize soiling

with blood. Placement of a sterile ventilation catheter in the distal airway across the surgical field has also been used to deliver HFPPV [11]. It should be noted that the use of the high-frequency oscillation ventilation, which is increasingly used in intensive care units, is not useful for airway surgery due to excessive movement of the airways produced by this modality [33].

Disadvantages of the use of high-frequency techniques include requirement for specialized ventilator equipment and technical difficulty in monitoring ventilation parameters. The variable positioning of ventilation catheters during airway surgery precludes the use of optimal sites for airway pressure monitoring. Peripheral airway pressures may be markedly different from those in the large airways due to gas trapping inherent to the use of high respiratory rates, short expiratory times, and expiratory flow limitation. Delivered breath volumes are nearly impossible to quantify with an open airway, therefore serial blood gas analysis is essential to detect hypoventilation. Provision for humidification of gases must be made for longer procedures to avoid drying of the airway mucosa and desiccation of secretions; this is a particular problem when jet techniques are used. All modes of high-frequency ventilation require that the delivery circuits have minimal compliance. Review of the HFV literature is notable for the variation in devices used in different clinical reports. Many ventilators and breathing circuits are institution specific, having been built in a hospital laboratory. A description of operating conditions is often lacking. Many devices are in fact hybrids, superimposing a high-frequency mode on conventional IPPV or displaying features of two forms of high-frequency ventilation. Similarly, many catheters used for the delivery of high frequency and jet ventilation are either institution specific or intended for other purposes such as urethral catheters or airway suction catheters, for example. There is inherent risk in the use of high flow, high pressure gas pulses in the airway, even more so when delivered at rapid rates. Catheter position and alignment within the tracheobronchial tree must be known at all times and is made more difficult by manipulation of the airway during surgery. Free egress of expired gas and adequate expiratory time must be maintained in order to avoid inadvertent hyperinflation and lung injury. Whereas continuous positive airway pressure is expected in HFV and is beneficial in maintaining lung recruitment, the use of higher ventilation rates and higher volumes may result in occult PEEP [31]. The resulting lung hyperinflation can lead to impedance of venous return and hemodynamic compromise, particularly if the chest is closed. Barotrauma and volutrauma in the form of pneumothorax, pneumomediastinum, and subcutaneous emphysema have been reported with all forms of high-frequency ventilation and with LFJV. The use of not only distal airway pressure monitoring, but automatic shutoff mechanisms to prevent further gas flow into the lungs in the event of high airway pressure is recommended [36].

While there are reports of the adaptation of volatile agent vaporizers for use with high-frequency ventilation [45], this is unnecessary as current practice offers satisfactory total intravenous anesthetic regimens (see Chap. 12). The use of short acting volatile agent using the high flows required of HFV is wasteful and difficult to scavenge.

Extraordinary Ventilation Strategies

Cardiopulmonary Bypass (CPB) and Extracorporeal Oxygenation (ECMO)

CPB without circulatory arrest was first used for resection of a carinal tumor in 1959 followed by reports of small series in both adults and children [46]. Then as now, systemic anticoagulation required for CPB may introduce formidable problems, notably intrapulmonary hemorrhage [4]. Currently, CPB is considered only under specific circumstances: tracheoplasty of long segments in small children in whom small airway caliber precludes other options [47], combined cardiac and pulmonary procedures for malignant disease in adults [48], the repair of complex tracheobronchial injuries [49], or when tracheal occlusion is imminent by a lesion unlikely to be bypassed by tracheotomy or rigid bronchoscopy [50]. More recent reports of tracheal reconstruction in pediatric [51] and adult patients [52] using extracorporeal membrane oxygenation (ECMO) have emphasized that this form of lung assist is amenable to peripheral rather than central vascular cannulation and reduced levels of anticoagulation. The practice of performing particularly complex tracheal reconstruction only in centers where extracorporeal support is available can be justified.

Spontaneous Ventilation

A departure from the use of neuromuscular relaxants and positive pressure ventilation, are case reports of a small number of patients allowed to breathe spontaneously throughout tracheal resection [53] and tracheoesophageal (TE) fistula repair [54]. Total intravenous anesthesia was provided with endotracheal oxygen insufflation. Some aspiration of blood and debris from the surgical field was noted. The reported patients were well oxygenated and stable despite moderate respiratory acidosis; however, it is unlikely that patients with significant limitation of pulmonary reserve would tolerate this approach. A pilot study of the feasibility of patients undergoing tracheal resection using cervical epidural anesthesia and remifentanil sedation was recently reported. The authors reported that the surgery was facilitated by the absence of any tube or catheters within the airway. They did not discuss what they would have done if a patient has suffered complete airway obstruction [55].

Hyperbaric Oxygenation

The use of hyperbaric oxygenation has been reported to supplement differential lung ventilation by conventional and

HFV modes when these methods failed in the repair of a large tracheal tear [56]. Hyperbaric conditions enhance oxygen delivery via increased oxygen dissolved in the plasma. This approach requires the performance of surgery within a hyperbaric chamber with compression of the entire surgical team and must be considered experimental.

Anesthesia Induction and Maintenance

Careful questioning of the patient will reveal position-dependent increase in airway obstruction, particularly intolerance to lying supine. Anesthetic induction may be performed in a sitting or semisitting position. Any difficulty encountered at previous intubation or bronchoscopy should be known to the team. All team members should be present. A clear, coordinated plan is required and ongoing communication is essential. All equipment anticipated for airway management should be ready and confirmed to be working.

When there is little or no tracheal obstruction, the induction of anesthesia, neuromuscular relaxation and intubation is performed as per the anesthesiologist's usual practice. In the presence of significant airway obstruction or stenosis, induction is followed by rigid bronchoscopy, dilation of tracheal stenosis, or debridement of tumor prior to placement of an orotracheal tube. A variety of anesthetic strategies have been described including airway topicalization and awake intubation, inhalational induction with volatile anesthetics, and intravenous induction agents with and without the use of neuromuscular relaxants [17]. Awake intubation is of questionable value in this circumstance, in patients with high stenosis, endotracheal tube placement is not possible and in those with lower lesions, the tube must shortly be removed for rigid bronchoscopy after the induction of general anesthesia. When an inhalation induction is chosen, currently sevoflurane is most often used. Complete preoxygenation/de-nitrogenation will take more than the usual time, often more than 5 min, due to restriction of spontaneous tidal volumes. In the setting of airway compromise, inhalation induction with a slowly increasing concentration of a volatile anesthetic in 100% oxygen will also take increased time. Patients often require some ongoing continuous positive airway pressure via the anesthetic circuit to maintain even modest tidal volumes. When a deep plane of anesthesia is achieved, a local anesthetic (often lidocaine) is applied to the vocal cords and upper airway prior to instrumentation. While this approach attempts to maintain the ability to turn off the anesthetic and to wake up the patient if difficulties are encountered, it is not without drawbacks. The decision to attempt airway dilation without the use of relaxant may make placement of the rigid bronchoscope considerably more difficult. If the patient breathes forcefully against a nearly obstructed airway as a very small bronchoscope fills the remaining lumen, the patient is put at risk of negative-pressure pulmonary edema. Another option

after inhalation induction is to use a short acting muscle relaxant (such as succinylcholine) to facilitate the introduction of the bronchoscope. Intravenous induction of anesthesia with the use of short or intermediate acting muscle relaxant to facilitate rigid bronchoscopy is described in many reports and is particularly appropriate when prior rigid bronchoscopy has been uneventful. This is the approach most often used in our center. However, it is clear that the decision of what induction agent to use and when to give a muscle relaxant and control the patient's ventilation must be made by the anesthesiologist and surgeon based on their assessment of the patient and their level of experience.

The sympathetic response to airway instrumentation may be reduced by the use of intravenous lidocaine (1–1.5 mg/kg) bolus prior to induction. For intravenous induction, a combination of propofol and an opioid (fentanyl boluses or a remifentanil infusion) is frequently used. Another choice of induction agent is Ketamine, an *N*-methyl d-aspartate receptor antagonist that produces dissociative anesthesia. Ketamine depresses ventilation less than many other sedative or general anesthetic drugs. It has the additional advantage of having bronchodilator and sympathomimetic effects and may contribute to the prevention of postincisional pain. Dexmedetomidine is a relatively new induction agent which has been reported to be useful for the management of the patient with a compromised airway [57]. After induction, the patient may be bag-mask ventilated until the introduction of the rigid bronchoscope, or a LMA may be placed. Once the tracheal obstruction is relieved, the trachea is intubated and positive pressure ventilation instituted. A dose of an intermediate acting muscle relaxant is usually given and provision is made for ventilation during the period of open airway.

Anesthesia may be maintained with an inhalational agent while the trachea is intact, but during cross-field ventilation, where there are frequent periods where the endotracheal tube is out of the airway and the inhaled anesthetic is not delivered to the patient. Many anesthesiologists will convert to a total intravenous technique with propofol with an opioid, often a remifentanil infusion at this stage. Similarly, intravenous anesthesia is used when high frequency and jet ventilation techniques are required.

Reconstruction of the Airway

When the airway is open, the surgeon is able to manipulate the endotracheal tube within the trachea. During distal cross-field ventilation, in order to easily retrieve the distal tip of the retracted orotracheal tube, the surgeon may affix a suture to the Murphy eye which remains in the surgical field and can be used to reposition the orotracheal tube when needed. If the orotracheal tube is damaged, specifically if the cuff is ruptured, it may be replaced if the trachea is still open. After removal of the connector of the new tube, the surgeon can insert the

pilot balloon within the tube lumen and pass the tube retrograde up the trachea into the oropharynx where it is retrieved by the anesthesiologist. During airway reconstruction, the use of uncut endotracheal tubes is recommended, as positioning distal to surgical anastomoses is frequently required. When the airway is closed, conventional positive pressure ventilation through the orotracheal tube is resumed.

When a Montgomery T-tube is left in the trachea, there are several ways to maintain ventilation. An inflated Fogarty catheter can remain in the proximal limb while positive-pressure ventilation is provided by the tracheotomy limb. This can be facilitated by the use of a multiport airway connector of the type used for a bronchial blocker. The multiport adaptor is connected to the tracheal limb of the T-tube via an endotracheal tube connector (from a 5.0 or 6.0 endotracheal tube) and the Fogarty catheter is placed in the proximal limb of the Montgomery T-tube via the side port [58]. Alternately, the surgeon will fit a small (usually 6.0 mm) endotracheal tube into the proximal limb. This press fit permits positive pressure ventilation via the proximal limb with the tracheotomy limb corked. With spontaneous ventilation reestablished, the endotracheal tube is removed by steady traction while the surgeon maintains the position of the T-tube with a clamp.

In upper and mid-tracheal resections, the head is flexed as the anastomosis is created to reduce anastomotic tension. The guardian ("chin") stitch is placed after skin closure, between the skin of the chin and the anterior chest (Fig. 13.2). Patients should be warned of this positioning (i.e., that their head will be flexed at the time of emergence) and all efforts should be made to maintain the flexed position during the postoperative period to avoid traction on the new repair.

Emergency After Airway Surgery

The resumption of sustained spontaneous ventilation is highly desirable. Prompt extubation is a priority after airway reconstruction to avoid positive pressure or endotracheal tube cuff trauma to the new anastomosis, which might predispose to dehiscence. Most patients breathe more comfortably in a sitting position, removing the weight of abdominal contents from the diaphragm and increasing the patient's functional lung capacity. The oropharynx is thoroughly suctioned, neuromuscular blockade is fully reversed, and the patient is extubated when awake, able to maintain patency of their upper airway and to mobilize secretions. A propofol infusion for the final stages of the procedure is useful, which permits rapid emergence to a wakeful state without agitation in most cases. It is important to avoid abrupt neck extension with possible traction injury to the anastomosis. The patient should be warned in advance of the need to maintain head flexion and the presence of the guardian stitch. Alternatively, the trachea may be extubated while the patient is still anesthetized, breathing spontaneously, and a laryngeal mask placed. This permits fiberoptic bronchoscopy and assessment of both the

anastomosis and vocal cord function. Emergence with the laryngeal mask in place provokes minimal airway irritation and coughing, the patient will often atraumatically remove the device themselves. A drawback of this approach is that the laryngeal mask is not always easily seated in the supraglottis, this technique is best reserved for patients who were easy to bag-mask ventilate.

Maintenance of normothermia is important, shivering increases oxygen consumption, which is particularly problematic if the patient's airway is compromised. Humidification of inhaled gases minimizes the inspissated airway secretions.

Reintubation after tracheal reconstruction may be difficult. After subglottic resection the patient's neck may be positioned in extreme flexion, the airway may be edematous and bloody, and there is potential for mechanical injury to the new anastomosis. If required, endotracheal tube repositioning is best accomplished under direct vision with a fiberoptic bronchoscope. When an airway stent is left in place, the trachea should not be blindly intubated from above. Telescoping of a small endotracheal tube into the stent may be possible using a bronchoscope. This technique should be applied with great care when a self-expanding metal stent has been placed for airway stenosis; the stents require several hours to completely expand. Insertion of an endotracheal tube may distort or dislodge the stent, especially if the balloon cuff becomes snagged. An LMA may be positioned above the stented airway, particularly if a short period of ventilatory assistance is required or to facilitate emergence from anesthesia. The airway with a Montgomery T-tube can be ventilated in several ways. The side arm protruding via a tracheal stoma will accommodate an endotracheal tube connector (from a 5.0 to 6.0-mm ETT), permitting connection to standard ventilation circuits. If positive pressure is required, the open upper limb must be obstructed to prevent loss of ventilating gas. The patient's mouth and nose may be manually held shut, packing may be placed in the pharynx, or an embolectomy catheter (Fogarty #14) may be directed into the upper limb via the side arm of the stent and the balloon inflated [59]. LFJV may also be initiated via the side arm [60].

Immediate Postoperative Complications Specific to Airway Surgery

In all surgical patients, residual anesthetics, analgesics, and neuromuscular blockade may contribute to hypoventilation, atelectasis, and poor mobilization of secretions, leading to postoperative respiratory compromise. Additional pulmonary complications may be a direct result of surgery to the airway. Airway obstruction should be suspected if the patient is in respiratory distress particularly if stridor is evident. Prior to emergence the tracheobronchial tree should be examined and any residual blood in the airway should be carefully removed; despite this, bleeding may be ongoing, or old clot may be mobilized from the lung periphery. Airway caliber may be further compromised by edema. Diuresis and corticosteroids

are used empirically; however, controlled studies of their use in airway surgery are entirely lacking. Dexamethasone is frequently chosen for its long duration of action, however several hours may be required after dosing (4–10 mg intravenously) for edema to subside. For many years, nebulized racemic epinephrine has been recommended for treatment of postintubation edema. The racemic form, which is an equal mixture of the dextro- and levo-isomers of epinephrine, is increasingly unavailable. The more commonly available 1% levo-epinephrine is proposed to be equally effective [61]. In our institution, 5 mL of 1:1,000 epinephrine is administered by nebulizer unless limited by tachycardia. Helium and oxygen mixtures provided by a nonrebreathing facemask may permit increased ventilation in patients with narrowed conducting airways and are useful as a supportive measure while definitive therapy is pursued. Breathing with airway obstruction may be viewed as breathing through an orifice, which creates turbulent flow. Under turbulent conditions, gas flow resistance varies inversely with density to the fifth power. The low density of helium permits a 1.5-fold increase in relative flow of the commercially available Heliox (70% helium/30% oxygen) over air and oxygen mixtures [62]. The high helium fraction required to significantly reduce the work of breathing precludes high delivered oxygen concentrations which may be undesirable if the patient has a low oxygen saturation. When airway compromise is refractory to medical therapy, reintubation may be required.

Pulmonary parenchymal injury may occur. In a review of cases of pulmonary edema associated with airway obstruction after surgery, more than 20% of cases were in adults being treated for airway tumor [63]. Spontaneous inspiratory efforts against an obstructed upper airway result in marked negative intrapleural and transpulmonary pressures, causing edema formation, usually within minutes. Laryngospasm is a frequent precursor. Bronchoscopic findings include pink frothy secretions and punctate hemorrhagic lesions throughout tracheobronchial tree [64]. Treatment is supportive and includes reestablishment of airway patency, oxygen supplementation, and diuresis; 85% of patients require reintubation, usually of short duration.

Pulmonary aspiration of acidic stomach contents is a particular concern during and after airway surgery where the trachea is not consistently protected by an endotracheal tube. Aspiration may occur at the time of airway manipulation, or after completion of the airway procedure. Patients with newly placed T-tubes may occur have difficulty closing their glottis. Laryngeal dysfunction can occur after suprathyroid release but is less common than after previously used thyrohyoid release procedures [65]. Swallowing dysfunction usually improves after a few days. Recurrent laryngeal nerve paralysis is possible after tracheal surgery. Chemoprophylaxis with antacids, H₂ blockers, and gastric prepulsants remains unproven in the prevention of the secondary lung injury of acid aspiration. Once aspiration has occurred, treatment is supportive; bronchoscopy for removal of particulate matter, and ventilation with positive end-expiratory pressure if indicated.

Tracheal Procedures with Specific Considerations

Two clinical scenarios present the challenge of a preexisting defect in the trachea prior to the induction of anesthesia: traumatic injury to the airway and TE fistula.

Airway Trauma

Iatrogenic airway injury may occur during airway instrumentation, most often the posterior membranous portion of the trachea. This may occur during intubation with a single lumen endotracheal tube or advancement of a bougie, bronchoscope, or other inflexible device. Injury during placement of a double-lumen tube is most frequently located in the membranous (posterior) trachea near the carina. If not noted intraoperatively, most injuries becoming apparent immediately after extubation. While small tears may be managed conservatively, urgent repair is required when significant clinical manifestations occur such as hemoptysis, dyspnea, or pneumomediastinum, or if bronchoscopic examination reveals gaping of the edges of the tear during respiration. Repair of injuries in the upper trachea may be possible via an extended cervicotomy, whereas thoracotomy is required for tears that extend lower in the airway [66]. Preoperative assessment is limited by the urgency of the procedure. Pulmonary function testing with spirometry is contraindicated as positive airway pressure will increase subcutaneous emphysema. Intubation of the patient for surgery is best accomplished under bronchoscopic guidance while the patient is breathing spontaneously, either awake with upper airway topicalization or after inhalation induction, until the lesion is bypassed. When a transtracheal approach is used the surgeon will make an anterior tracheotomy and pass a small endotracheal tube distally to be used intermittently for ventilation. The repair is performed during periods of apnea when the cross-field tube is withdrawn. Repairs via thoracotomy may be managed with a small diameter single-lumen endobronchial tube guided under direct vision to the side contralateral to the tear. A double lumen tube may be used but has a larger diameter which may make placement more difficult and may impede the surgical repair.

Injury to the conducting airways may be a result of blunt or penetrating trauma, often other injuries are present. Respiratory distress and subcutaneous emphysema are the most common physical findings [67]. Approximately, 6% of penetrating neck injuries involve tracheal trauma as compared to less than 1% of patients with penetrating chest injuries. Most patients with blunt trauma severe enough to cause a tracheal tear do not survive long enough to present to hospital. But in those who do, cervical spine injury is common and must be considered when securing the airway. The disruption of the trachea is most likely to occur within 2 cm of the carina. Airway control beyond the injury is required and intubation with the aid of fiberoptic bronchoscopy in the spontaneously

ventilating awake patient is recommended both to inspect the injury to secure ventilation. When lower airway injury is identified endobronchial intubation of side contralateral to the injury may be desirable. Trauma cases are particularly fraught with technical difficulties, patient agitation, and competing medical concerns. If the initial plan for securing the airway fails, an alternate plan should be identified. A surgical tracheostomy is useful in injuries of the cervical trachea. But if the tear is intrathoracic, tracheostomy is of no benefit. CPB via femoral cannulae has been described to provide lifesaving oxygenation and ventilation in such scenarios, but this is certainly not available in all trauma centers and has the significant drawback of the requirement for full anticoagulation of a polytrauma patient [68].

Tracheoesophageal (TE) Fistula

Congenital TE fistula is recognized in the neonatal period. Adults may acquire such a lesion from trauma, neoplasia, or radiotherapy. In cases of TE fistula, contamination of the airway with gastric contents and preexisting pulmonary injury likely will have occurred, resulting in preoperative pneumonitis. Positive pressure ventilation is avoided prior to securing the airway as gastric insufflation may result in increased intrathoracic pressure, difficult ventilation, and impaired venous return [69]. Placement of an endotracheal tube beyond the fistula while maintaining spontaneous ventilation is recommended. A novel variation of this strategy was described in an adult who presented for resection of a large carinal TE fistula. To independently isolate each lung, two 5.0 mm micro-laryngoscopy endotracheal tubes were placed sequentially in each bronchus following inhalation induction of anesthesia using sevoflurane. Conventional IPPV was then initiated [70] (see Chap. 17, Fig. 17.10b)

Pediatrics

Congenital tracheal stenosis in infants and children typically occur in the presence of complete tracheal rings and may involve significant lengths of the trachea. Not infrequently these lesions are associated with cardiovascular anomalies which also require repair, most often a pulmonary artery sling. Surgical reconstruction of long-segment tracheal stenoses has been described with a number of techniques including simple resection, incision, and patching with pericardium, rib cartilage or tracheal autograft, and slide tracheoplasty all performed via median sternotomy [71]. Slide tracheoplasty is performed by dividing the stenotic trachea at midpoint, incising the proximal and distal narrowed segments vertically on opposite anterior and posterior surfaces and sliding these together. The advantage of this approach is that only fully vascularized, cartilage supported tissue is used which permits early extubation of many patients. There remains some debate among surgeons which procedure should be performed, whether CPB is always required when only airway reconstruction is performed, and if

cardiovascular repair is required, should the procedures be staged or performed as a single operation. These surgeries are performed in highly specialized centers, and early referral is recommended to avoid complications associated with lengthy preoperative periods of mechanical ventilation (see also Chap. 39).

Management of the Patient with a T-Tube

A T-tube may be placed for a finite period of time to allow an upper airway prone to malacia or scarring to heal and stabilize, or in some cases becomes essentially permanent airway support. Patients with T-tubes may require airway examination, replacement, or adjustment of their T-tube or surgery unrelated to their airway. They present a significant challenge to the anesthesiologist. When a patient with a T-tube *in situ* requires a general anesthetic, the risk of aspiration should be considered. If the procedure is elective the upper airway can be controlled by a LMA either with spontaneous or controlled ventilation, with the external tracheostomy limb capped. Alternatively, the use of a well-seated laryngeal mask which was then capped to block the escape of from the proximal tracheal limb, while ventilating the patient via the tracheostomy limb has been described [72]. Other methods of ventilation through the T-tube offer only partial airway protection from aspiration such as the placement of a Fogarty catheter through the tracheotomy limb into the proximal limb to block egress of gas into the upper airway, with simultaneous ventilation through the tracheotomy limb. Awake fiberoptic telescoping of a small endotracheal tube into the proximal tracheal limb of the T-tube has been described, but aspiration around the T-tube is still possible. In a full stomach situation, there is a report of awake fiberoptic placement of a 5-mm microlaryngoscopy tube completely through the trachea proximal and distal limbs of the T-tube then inflating the cuff in the distal trachea [73]. Adult T-tube sizes vary from 8 to 16 mm external diameter. This approach may only be possible with the larger sizes. Finally, the T-tube can be removed, ideally with the help of the patient's surgeon, and replaced by a tracheotomy tube. If the tracheotomy is left for any length of time, the patient could suffer a recurrence of their airway compromise. They would also need another general anesthetic for replacement of the T-tube.

Clinical Case Discussion

A 30-year-old-male is scheduled to have a thoraco-lumbar laminectomy in the prone position for a burst fracture of L1. The patient is obese (height, 170 cm, weight 93 kg, BMI 32). The patient's past history is significant for a head injury in a motor vehicle accident at age 15 with prolonged (3 weeks) intubation and ventilation and full neurological recovery. The patient subsequently had multiple general anesthetics for rigid

and flexible bronchoscopy for tracheal stenosis and a tracheal resection at age 17. He had no problems with anesthesia and has had no medical follow-up since that surgery. Other history is unremarkable.

The patient describes limitation of routine activities; he can only climb one flight of stairs without stopping to rest, and two-pillow orthopnea, which he attributes to his obesity. On physical examination, he has inspiratory and expiratory stridor at rest. There are no other significant findings on physical examination. He does not appear to be a difficult intubation.

Question

Apart from routine laboratory examinations, what specific preoperative investigations should be requested?

Answer

The source of the patient's dyspnea needs to be identified and managed if possible. The patient should have a chest X-ray, CT scan of his trachea, pulmonary function tests, arterial blood gases, ECG, and transthoracic echocardiography.

ECG, echocardiogram, and blood gases are normal. Pulmonary function tests reveal a severe limitation of peak expiratory and inspiratory flows (FEV1=50% predicted) with a normal DLCO and no response to bronchodilators. CT scan shows a mid-tracheal stenosis with a length of 3 cm and the narrowest cross-section area measures 5×15 mm (the CT image is similar to Fig. 17.3).

Question

What the optimal anesthetic management for the prone laminectomy?

Answer

A thoracic surgeon was consulted and agreed that a rigid bronchoscopy and tracheal dilation was indicated for this patient and this could be performed during the same anesthetic.

After placement of routine monitors and a radial arterial line, anesthesia was induced with propofol and the ability to bag-mask ventilate the patient was confirmed with the thoracic surgeon present and prepared for rigid bronchoscopy. Remifentanil and succinylcholine were then administered and direct laryngoscopy was performed and the vocal cords and upper trachea sprayed with 3 mL of 4% lidocaine. Anesthesia was then maintained with propofol and remifentanil infusions and rocuronium boluses. The thoracic surgeon performed a rigid bronchoscopy, initially with a 4-mm diameter bronchoscope, and the patient's trachea was serially dilated until a 9-mm rigid bronchoscope could be passed. Ventilation was maintained with LFJV during the bronchoscopy. Then the patient was intubated with a 7-mm armored ETTube during direct laryngoscopy and the position of the distal ETT tip

beyond the stenosis and above the carina confirmed with flexible fiberoptic bronchoscopy (FOB).

The patient was then positioned prone for the laminectomy and the position of the ETT reconfirmed with FOB. Anesthesia was maintained with sevoflurane, and boluses of fentanyl and rocuronium. Dexamethasone was administered to decrease airway edema.

Question

At the end of the 4 h laminectomy, how should the patient's airway be managed?

Answer

The patient was returned the supine position with his head elevated 30°. Neuromuscular blockade was reversed and the patient allowed to resume spontaneous ventilation with 2 MAC sevoflurane. The ETT was then removed and replaced with a LMA. FOB via the LMA revealed minor tracheal mucosal trauma at the site of dilation but the airway caliber was maintained without tracheomalacia. The sevoflurane was then discontinued and the LMA removed in the operating room after the patient became responsive.

Question

What are the major anesthetic options in this case?

Answer

1. Regional anesthesia (e.g., spinal) is an option but the duration of surgery makes it a questionable choice in this case and the problems of managing the anesthetic in the prone position if the block wore off are considerable.
2. The use of an LMA for controlled ventilation for the entire procedure has been described for a similar case [74]. However, this does not address the underlying problem of the tracheal stenosis and a prolonged general anesthetic in the prone position without a secure airway is not the best option.

References

1. Belsey R. Resection and reconstruction of the intrathoracic trachea. *Br J Surg.* 1950;38:200–8.
2. Barclay RS, McSwan N, Welsh TH. Tracheal reconstruction without the use of grafts. *Thorax.* 1957;12:177–83.
3. Grillo HC, Bendixen HH, Gephart T. Resection of the carina and lower trachea. *Ann Surg.* 1963;158:889–95.
4. Geffin B, Bland J, Grillo HC. Anesthetic management of tracheal resection and reconstruction. *Anesth Analg.* 1969;48:884–90.
5. Grillo HC, Mathisen DJ. Surgical management of tracheal strictures. *Surg Clin North Am.* 1988;68:511–24.
6. Miura T, Grillo HC. The contribution of the inferior thyroid artery to the blood supply of the human trachea. *Surg Gynecol Obstet.* 1966;123:99–102.
7. Merritt RE, Mathisen DJ. Tracheal resection. In: Patterson GA, Cooper JD, Deslauriers J, et al., editors. *Pearson's thoracic and esophageal surgery.* 3rd ed. Philadelphia: Churchill Livingstone; 2008. p. 377–82.
8. Macchiarini P, Jungebluth P, Go T, et al. Clinical transplantation of a tissue-engineered airway. *Lancet.* 2008;372:2023–30.
9. dePerrot M, Fadel E, Darteville P. Carinal resection. In: Patterson GA, Cooper JD, Deslauriers J, et al., editors. *Pearson's thoracic and esophageal surgery.* 3rd ed. Philadelphia: Churchill Livingstone; 2008. p. 383–92.
10. Wright C, Grillo H, Wain JC, et al. Anastomotic complications after tracheal resection: prognostic factors and management. *J Thorac Cardiovasc Surg.* 2004;128:731–9.
11. Young-Beyer P, Wilson RS. Anesthetic management for tracheal resection and reconstruction. *J Cardiothorac Anesth.* 1988;2: 821–35.
12. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J.* 2005;26:948–68.
13. Tomori Z, Widdicombe JG. Muscular, bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract. *J Physiol.* 1969;200:25–49.
14. Hill AJ, Feneck RO, Underwood SM, et al. The haemodynamic effects of bronchoscopy, comparison of propofol and thiopentone with and without alfentanil pretreatment. *Anaesthesia.* 1991;46:266–70.
15. dePerrot M, Fadel E, Mercier O, et al. Long term results after carinal resection for carcinoma. *J Thorac Cardiovasc Surg.* 2006;131:81–9.
16. Licker M, Schweizer A, Nicolet G, et al. Anesthesia of a patient with an obstructing tracheal mass: a new way to manage the airway. *Acta Anaesthesiol Scand.* 1997;41:34–9.
17. Pinsonneault C, Fortier J, Donati F. Tracheal resection and reconstruction. *Can J Anesth.* 1999;46:439–47.
18. Grillo HC, Mathisen DJ. Cervical exenteration. *Ann Thorac Surg.* 1990;49:401–11.
19. Fischler M, Troche G, Guerin Y, et al. Evolution des techniques d'anesthesie pour resection-anastomose de trachee. *Ann Fr Anesth Rèanim.* 1988;7:125–7.
20. Conacher ID, Velasquez H, Morrice DJ. Endobronchial tubes – a case for re-evaluation. *Anaesthesia.* 2006;61:587–9.
21. Hannallah MS. The optimal breathing tube for tracheal resection and reconstruction. *Anesthesiology.* 1995;83:419–22.
22. Theman TE, Kerr JH, Nelems JM, et al. Carinal resection, a report of two cases and a description of the anesthetic technique. *J Thorac Cardiovasc Surg.* 1976;71:314–9.
23. Sanders RD. Two ventilating attachments for bronchoscopes. *Del Med J.* 1967;39:170–3.
24. Lee P, English ICW. Management of anesthesia during tracheal resection. *Anaesthesia.* 1974;29:305–10.
25. Ellis RH, Hinds CJ, Gadd LT. Management of anaesthesia during tracheal resection. *Anaesthesia.* 1976;31:1076–9.
26. McClish A, Deslauriers J, Beaulieu M, et al. High-flow catheter ventilation during major tracheobronchial reconstruction. *J Thorac Cardiovasc Surg.* 1985;89:508–12.
27. Baraka A. Oxygen-jet ventilation during tracheal reconstruction in patients with tracheal stenosis. *Anesth Analg.* 1977;56:429–32.
28. Clarkson WB, Davies JR. Anaesthesia for carinal resection. *Anaesthesia.* 1978;33:815–7.
29. Carlon GC, Kahn RC, Howland WS, et al. Clinical experience with high frequency ventilation. *Crit Care Med.* 1981;9:1–3.

30. Howland WS, Carlon GC, Goldiner PL, et al. High-frequency jet ventilation during thoracic surgical procedures. *Anesthesiology*. 1987;67:1009–12.
31. Sjostrand U. High-frequency positive-pressure ventilation: a review. *Crit Care Med*. 1980;8:345–51.
32. Glenski JA, Crawford M, Rehder K. High-frequency, small volume ventilation during thoracic surgery. *Anesthesiology*. 1980;59:577–80.
33. Carlon GC, Griffin J, Ray Jr C. High-frequency jet ventilation in experimental airway disruption. *Crit Care Med*. 1983;11: 353–5.
34. Beamer WC, Prough DS, Royster RL, et al. High-frequency jet ventilation produces auto-PEEP. *Crit Care Med*. 1984;12:734–8.
35. Froese AS, Bryan AC. High frequency ventilation. *Am Rev Respir Dis*. 1987;135:1363–7.
36. Adelsmayr E, Keller C, Erd G, et al. The laryngeal mask and high-frequency jet ventilation for resection of high tracheal stenosis. *Anesth Analg*. 1998;86:907–10.
37. Magnusson L, Lang FJW, Monnier P, et al. Anaesthesia for tracheal resection: report of 17 cases. *Can J Anaesth*. 1997; 44:1282–6.
38. Watanabe Y, Murakami S, Iwa T, et al. The clinical value of high-frequency jet ventilation in major airway reconstructive surgery. *Scand Thorac Cardiovasc Surg*. 1988;22:227–31.
39. Perera ER, Vidic DM, Zivot J. Carinal resection with two high-frequency jet ventilation delivery systems. *Can J Anaesth*. 1993;40:59–63.
40. Biro P, Hegi TR, Weder W, et al. Laryngeal mask airway and high-frequency jet ventilation for the resection of a high-grade upper tracheal stenosis. *J Clin Anesth*. 2001;13:141–3.
41. Eriksson I, Nilson LG, Nordstrom S. High-frequency positive-pressure ventilation during transthoracic resection of tracheal stenosis and during preoperative bronchoscopic examination. *Acta Anaesth Scand*. 1975;19:113–7.
42. El-Baz N, Holinger L, El-Ganzouri A. High-frequency positive-pressure ventilation for tracheal reconstruction supported by tracheal T-tube. *Anesth Analg*. 1982;61:796–800.
43. El-Baz N, El-Ganzouri A, Gottschalk W, et al. One-lung high frequency positive pressure ventilation for sleeve pneumonectomy: an alternative technique. *Anesth Analg*. 1981;60:683–6.
44. El-Baz N, Jensik R, Penfield Faber L, et al. One-lung high-frequency ventilation for tracheoplasty and bronchoplasty: a new technique. *Ann Thorac Surg*. 1982;34:564–7.
45. Baraka A, Mansour R, Jaoude CA, et al. Entrainment of oxygen and halothane during jet ventilation in patients undergoing excision of tracheal and bronchial tumors. *Anesth Analg*. 1986;65:191–4.
46. Louhimo I, Leijala M. Cardiopulmonary bypass in tracheal surgery in infants and small children. *Prog Pediatr Surg*. 1987; 21:58–63.
47. Benca JF, Hickey PR, Dornbusch JN, et al. Ventilatory management assisted by cardiopulmonary bypass for distal tracheal reconstruction in a neonate. *Anesthesiology*. 1988;68:270–1.
48. Ernst M, Koller M, Grobholtz R, et al. Both atrial resection and superior vena cava replacement in sleeve pneumonectomy for advanced lung cancer. *Eur J Cardiothorac Surg*. 1999;15: 530–4.
49. Symbas PN, Justicz AG, Ricketts RR. Rupture of the airways from blunt trauma: treatment of complex injuries. *Ann Thorac Surg*. 1992;54:177–80.
50. Wilson RF, Steiger Z, Jacobs J, et al. Temporary partial cardiopulmonary bypass during emergency operative management of near total tracheal occlusion. *Anesthesiology*. 1984;61:103–6.
51. Angel C, Murillo C, Zwischenberger J, et al. Perioperative extracorporeal membrane oxygenation for tracheal reconstruction in congenital tracheal stenosis. *Pediatr Surg Int*. 2000;16:98–101.
52. Walles T, Steger V, Wurst H, et al. Pumpless extracorporeal gas exchange aiding central airway surgery. *J Thorac Cardiovasc Surg*. 2008;136:1372–4.
53. Vyas AB, Lyons SM, Dundee JW. Continuous intravenous anaesthesia with Althesin for resection of tracheal stenosis. *Anaesthesia*. 1983;38:132–6.
54. Joyst GM, Chui PT, Mainland P, et al. Total intravenous anaesthesia and endotracheal oxygen insufflation for repair of tracheoesophageal fistula in an adult. *Anesth Analg*. 1996;82:661–3.
55. Macchiarini P, Rovira I, Ferrarello S. Awake upper airway surgery. *Ann Thorac Surg*. 2010;89:387–91.
56. Ratzenhofer-Komenda B, Offner A, Kaltenbock F, et al. Differential lung ventilation and emergency hyperbaric oxygenation for repair of a tracheal tear. *Can J Anesth*. 2000;47:169–72.
57. Ramsay MAE, Saha D, Hebel RF. Tracheal resection in the morbidly obese patient: the role of dexmedetomidine. *J Clin Anesth*. 2006;18:452–4.
58. Kailash F, DaSilva SL, Block FE. A novel approach to maintain positive pressure ventilation during difficult T-tube placement. *Can J Anesth*. 2009;56:709–10.
59. Lane GA, Steude G, Pashley NRT. Anesthesia for a patient with a tracheal T-tube stent. *Anesth Analg*. 1981;60:218–20.
60. Baraka A, Muallem M, Noueihid R, et al. Oxygen jet ventilation of patients with tracheal T-tube. *Anesth Analg*. 1982;61:622–5.
61. Nutman J, Brooks LJ, Deakins KM, et al. Racemic versus l-epinephrine aerosol in the treatment of postextubation laryngeal edema: results from a prospective, randomized, double-blind study. *Crit Care Med*. 1994;22:1591–4.
62. Doyle DJ, O'Grady KF. Physics and the airway: essentials for the clinician. The difficult airway I. *Anesthesiol Clin North Am*. 1995;13:277–86.
63. Lang SA, Duncan PG, Shepard DAE, et al. Pulmonary oedema associated with airway obstruction. *Can J Anaesth*. 1990;37:201–4.
64. Koch SM, Abramson DC, Ford M, et al. Bronchoscopic findings in post-obstructive pulmonary oedema. *Can J Anaesth*. 1996;43:73–6.
65. Grillo HC, Donahue DM, Mathisen DJ, et al. Postintubation tracheal stenosis: treatment and results. *J Thorac Cardiovasc Surg*. 1995;109:486–9.
66. Mussi A, Ambrogi MC, Menconi G, et al. Surgical approaches to membranous tracheal wall lacerations. *J Thorac Cardiovasc Surg*. 2000;120:115–20.
67. Devitt JH, Boulanger BR. Lower airway injuries and anaesthesia. *Can J Anaesth*. 1996;43:148–59.
68. Abernathy JH, Reeves ST. Airway catastrophes. *Curr Opin Anesthesiol*. 2010;23:41–6.
69. Salem MR, Wong AY, Lin YH, et al. Prevention of gastric distension during anesthesia for newborns with tracheoesophageal fistulas. *Anesthesiology*. 1973;38:82–5.
70. Au CL, White SA, Grant RP. A novel intubation technique for tracheoesophageal fistula in adults. *Can J Anesth*. 1999;46:688–92.
71. Manning PB, Rutter MJ, Border WL. Slide tracheoplasty in infants and children: risk factors for prolonged postoperative ventilatory support. *Ann Thorac Surg*. 2008;85:1187–92.

72. Agrawal S, Payal YS, Sharma JP, et al. Montgomery T-tube: anesthetic management. *J Clin Anesth.* 2007;19:135–7.
73. Wouters KMA, Byreddy R, Gleeson M, et al. New approach to anesthetizing a patient at risk of pulmonary aspiration with a Montgomery T-tube in situ. *Br J Anaesth.* 2008;101:354–7.
74. Isono S, Kitamura Y, Asai T, Cook TM. Case scenario: perioperative airway management of a patient with tracheal stenosis. *Anesthesiology.* 2010;112:970–8.
75. Hantler C, Wildes TS, Andritsos M. Anesthesia for airway surgery. In: Patterson AG, editor. *Pearson's thoracic and esophageal surgery.* Elsevier; 2008. p. 211–30.

14

Anesthesia for Patients with Mediastinal Masses

Chih Min Ku

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Key Points

- Patients with anterior mediastinal masses can develop major airway and cardiovascular compression under general anesthesia, which can be fatal.
- Patients who are symptomatic or have significant compression of these vital structures on CT scans are likely at high risk.
- Where possible, diagnostic procedures should be undertaken under local anesthesia.
- Understanding the relation of the mediastinal mass to vital cardiorespiratory structures, careful preoperative assessment of the patient, discussion with the surgeon, meticulous planning, and preparation for possible perioperative complications related to compression of the major airways and vascular structures are key to successful management.
- Useful strategies to consider include awake fiberoptic intubation, maintenance of spontaneous ventilation, avoidance of muscle relaxants, intubation distal to the airway compression, positioning changes, immediate availability of rigid bronchoscopy, and elective cardiopulmonary bypass in extreme cases.

- A careful anesthetic plan that is not irreversible is likely to result in a good outcome.

Introduction

Mediastinal masses are an uncommon entity. They constitute a heterogeneous group of benign and malignant tumors. The anesthesiologist may provide perioperative care to patients undergoing diagnostic and therapeutic procedures. They can present formidable challenges as mediastinal masses, especially those located in the anterior mediastinum, can cause perioperative morbidity and mortality by causing major airway and vascular compression, which may be exacerbated under general anesthesia. There are numerous case reports of fatal or near fatal complications associated with anesthesia for patients with anterior mediastinal masses [1–5]. Understanding the nature of the mediastinal mass in relation to vital structures, its pathophysiology, careful preoperative assessment of the patient, discussion with the surgeon, and being prepared for management of cardiorespiratory complications related to compression of the trachea and vascular structures are key to successful management.

Anatomy and Pathology

The mediastinum can be divided into four compartments: superior, anterior, middle, and posterior (Fig. 14.1). The mediastinum is bound by the thoracic inlet superiorly, the diaphragm inferiorly, mediastinal pleura laterally, sternum anteriorly, and the vertebral column posteriorly. The superior mediastinum extends from the thoracic inlet to a plane extending from the sternomanubrial junction to the inferior aspect of the fourth thoracic vertebra. The anterior mediastinum is bound anteriorly by the sternum and posteriorly by the pericardium. The middle compartment is bound anteriorly and posteriorly by the pericardium. The posterior mediastinum extends from the posterior pericardium to the anterior longitudinal ligament [6]. Some authors divide the mediastinum into three compartments [7, 8]. Table 14.1 shows the typical masses in the various mediastinal compartments [6, 8]. Most masses are located in the anterior mediastinum. In adults, the common pathologies include thymoma, lymphoma, and germ cell tumor. In the pediatric population, lymphoma, PNET, and neuroblastoma are more common [9].

Anterior mediastinal masses are more likely to cause severe cardiorespiratory problems due to their proximity and relation to the major airway and cardiovascular structures. Any compressive effects can be exacerbated under general anesthesia.

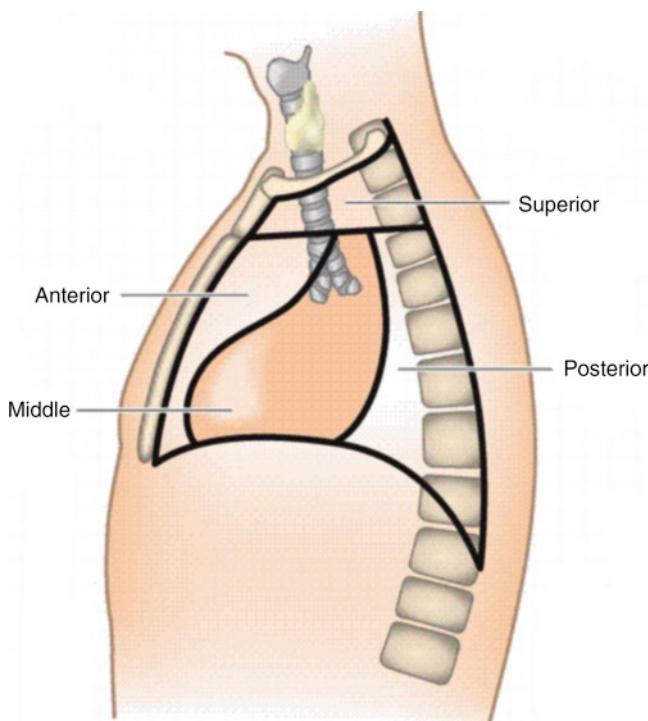


FIG. 14.1. Anatomic location of the four compartments of the mediastinum (reprinted from Warren [6] with permission).

TABLE 14.1. Masses in the mediastinal compartments.

Superior	Retrosternal thyroid Thymoma Thymoma Lymphoma Germ cell tumor Thymic cyst Parathyroid adenoma Bronchogenic cyst Cardiac/vascular structure Benign adenopathy Lymphoma Metastases Esophageal mass Hiatal hernia Neurogenic tumor Spine lesions
Anterior	
Middle	
Posterior	

Clinical Presentation

Tracheobronchial obstruction, superior vena cava syndrome, right heart and pulmonary vascular compression, and systemic syndromes, e.g., myasthenia gravis and thyroid disease are some of the common presentations of mediastinal masses [10]. The patient can also be asymptomatic.

Patients with tracheobronchial obstruction may complain of dyspnea, noisy breathing, nonspecific cough, and chest discomfort. These symptoms may be worse in certain positions, especially the supine position. They may find lying in certain positions more uncomfortable. Signs may include tachypnea, stridor, rhonchi, and decreased breath sounds, which may also be positional in nature. Physical examination is usually unremarkable. The severity of a patient's respiratory symptoms may not correlate with the degree of airway obstruction. Patients with severe respiratory symptoms may have significant decreases in tracheal cross-sectional area [11]. However, asymptomatic pediatric patients have developed airway obstruction during anesthesia [12–14]. Children may present with symptoms of airway obstruction earlier than adults because they have a smaller tracheal diameter and small decreases in tracheal diameter result in large decreases in cross-sectional area and increases in airway resistance [10].

Superior vena cava syndrome, due to obstruction of venous drainage in the upper thorax, may present as dyspnea, CNS symptoms like headache, visual disturbance, altered mentation, dilated collateral veins in the upper body and edema of the face, neck, and arms. Right heart and pulmonary vascular compression can present as dyspnea, syncope during a forced Valsalva maneuver [15], arrhythmias, and cardiac murmur. Symptoms may mimic those of tracheobronchial obstruction. Hence it is important to look for the relation of the mass to the tracheobronchial tree, right heart, and pulmonary vasculature in the radiology scans.

Preoperative Evaluation

The most important aim of preoperative investigation is to identify the size, the relations of the mediastinal mass to the tracheobronchial tree and vital vascular structures, and the location and extent of any compressive effects.

This is best done by radiological studies, mainly chest radiographs and CT scans. CT scans of the thorax provide accurate assessment of the tumor, its nature, size, extent, location, relations to the tracheobronchial tree and major cardiovascular structures, and airway diameters [16]. They are most useful for determining the precise level and extent of tracheobronchial or cardiovascular compression, and this information is essential for formulating the anesthetic plan.

MR imaging is not used routinely. However, it is useful in the diagnosis of neurogenic and vascular lesions, especially when the use of contrast material is contraindicated.

Transthoracic echocardiography can be considered if there is any suspicion of compression or invasion of cardiovascular structures [1], or if a significant pericardial effusion is identified on the CT scan.

Lung function tests and flow volume loops have been used, but their value in the assessment of mediastinal tumors is doubtful. Flow volume loops have been recommended in preoperative evaluation [17]. However, despite their purported ability to quantify the degree of impairment and differentiate extrathoracic from intrathoracic obstruction [18, 19], studies have shown that they correlate poorly with the degree of airway obstruction [20] and do not alter the anesthetic technique [21].

Surgical Approaches

Surgical procedures may be diagnostic or therapeutic. Diagnostic procedures are for the procurement of tissue for biopsy, in order to establish a histological diagnosis and guide treatment. Percutaneous CT-guided needle biopsy, done under local anesthesia, is a safe and cost-effective way of obtaining adequate tissue for histological diagnosis [22]. Other diagnostic procedures that can be done under LA include biopsy of an extrathoracic mass, anterior mediastinotomy [23], anterior mediastinoscopy [24], and endobronchial ultrasound-guided transbronchial needle aspiration. Most mediastinal masses require surgical resection. This can be done safely even if they have invaded surrounding structures [25]. Chemotherapy or radiotherapy may be used for Hodgkin lymphomas. The main surgical approaches include sternotomy, thoracotomy, cervical mediastinoscopy, anterior mediastinoscopy, and video-assisted thoracoscopic surgery. Occasionally, the patient may present for a surgery unrelated to the mediastinal mass [23]. Patients with undiagnosed mediastinal masses undergoing unrelated surgery present extra challenges [26].

Preoperative Treatment

Patients with mediastinal masses causing significant respiratory or cardiovascular compression are at high risk of cardiopulmonary collapse under general anesthesia. They may benefit from preoperative treatment of the mediastinal mass with steroids, chemotherapy, or radiotherapy, in order to shrink the tumor and alleviate the obstruction [11, 27–30]. Preoperative radiation therapy due to severe clinical or radiological findings has been associated with a decrease in postoperative respiratory complications [31]. However, tumor shrinkage can affect the accuracy of a histological diagnosis and cause diagnostic confusion. There is considerable controversy over the role of pretreatment. It has been reported that tissue diagnosis was not affected if biopsies were taken within 72 h of starting treatment [28]. Hack et al. found that a clear diagnosis was made in 95% of children considered high risk who were given steroids prior to diagnosis [29]. Ferrari et al. believe that pretreatment affects accuracy of histological diagnosis and prefer to acquire a tissue diagnosis before starting treatment. In their series, which included high-risk patients, 9 of the 44 pediatric patients who required general anesthesia were symptomatic preoperatively. No pretreatment was given before general anesthesia. There was no perioperative death or permanent injury, despite the occurrence of perioperative cardiorespiratory compromise, which was successfully managed [32]. The risk of intraoperative cardiopulmonary collapse during a diagnostic procedure, where general anesthesia is necessary, must be weighed carefully against the risk of diagnostic inaccuracy of preoperative treatment, in patients with large anterior mediastinal masses causing considerable cardiopulmonary compromise.

Anesthetic Management

Options include local anesthesia or general anesthesia, depending on the nature of the surgery. Discussion with the surgeon regarding the type of tumor, presence and degree of tracheobronchial and cardiovascular compression, the surgical approach, type of anesthesia, and other options, is paramount.

Biopsy under local anesthesia is ideal for large anterior mediastinal masses, especially if the patient is symptomatic [11]. This may be difficult in children. Pretreatment of large tumors can be considered, bearing in mind the possible adverse effects of pretreatment on the accuracy of histological diagnosis.

The dangers of general anesthesia in patients with mediastinal masses have been emphasized by many authors [33–36]. Postulated reasons for the dangers of general anesthesia include the fact that lung volume is reduced under general anesthesia and relaxation of bronchial smooth muscle leads to greater compressibility of the airway from the overlying mass. Muscle relaxant-induced paralysis of the diaphragm reduces

the normal transpleural pressure gradient which dilates the airway. This decreases the caliber of the airways and enhances the effect of extrinsic compression [1].

For procedures under general anesthesia, standard monitors and good intravascular access are routine. Invasive monitoring of blood pressure is preferably established preinduction, in view of possible hemodynamic instability. The necessity of insertion of central venous catheter and the use of transesophageal echocardiography depend on the patient's comorbidities and nature of the mediastinal mass.

Induction and Intubation

In patients with tracheobronchial obstruction undergoing GA, the technique of induction and intubation depends on the site and extent of tracheobronchial obstruction. This can include awake fiberoptic intubation [37–39], inhalational induction [12, 32], and routine intravenous induction. Awake fiberoptic intubation allows assessment of the level and degree of tracheobronchial compression [37–39]. The least obstructed bronchus can also be identified [38] to permit planning of subsequent rescue procedures which may be necessary later. Awake fiberoptic intubation is likely the safest technique of airway management because the patient is breathing spontaneously without any of the deleterious effects of general anesthesia. It is the most reversible technique, can be aborted at any point, and can be done in pediatric patients as well [37]. If CT scans suggest intubation distal to the obstruction is possible, awake fiberoptic intubation is probably the safest technique in patients who are symptomatic from large anterior mediastinal masses causing significant or distal tracheobronchial obstruction. Inhalational induction, if contemplated, should be used judiciously, as a partially obstructed respiration can generate large negative pressures which can further collapse a compressed trachea. An inhalational induction can actually precipitate airway obstruction [37]. Aborting a semi-obstructed inhalation induction midcourse is potentially difficult and hazardous. The likelihood of supraglottic upper airway obstruction, which may further compound the problem, should be carefully assessed before embarking on this technique. It may also have limitations in the obese patient. If a patient has no clinical or radiological evidence of airway or cardiovascular compression from a small mediastinal mass, a routine intravenous induction with or without ketamine can be performed carefully. Extra care must be taken in children because asymptomatic or minimally symptomatic children have experienced severe complications during anesthesia [12–14, 27, 40].

Maintenance of spontaneous ventilation and avoidance of paralysis are advocated to avoid complete airway obstruction by preserving normal transpulmonary pressure and maintaining airway patency [30, 41]. If paralysis is used, muscle relaxants with short duration should be given only when a definite airway and the ability to ventilate are certain. Problems with

ventilation have often been encountered after paralysis [1, 38] despite the apparent prior ability to control ventilation [1].

If intubation is planned, the anesthesiologist aims to intubate distal to the level of tracheobronchial obstruction, which may occasionally entail endobronchial intubation [12]. Endotracheal tubes long enough to intubate a mainstem bronchus if necessary [37, 42], endobronchial tubes, and microlaryngeal tubes [12] should be immediately available. Occasionally, when intubation distal to the tracheobronchial obstruction is not possible, other measures which may be useful include distal jet ventilation catheter via a proximally intubated trachea and rigid bronchoscopy [1, 42]. Rigid bronchoscopy, which should always be on standby with a skilled surgeon, allows assessment of the most patent airway, provides a conduit for jet ventilation, and stenting of the airway, if feasible. The futility of controlling ventilation of a patient with distal tracheobronchial obstruction through a proximal airway has been described [1]. Occasionally, intubation can precipitate or exacerbate obstruction, which may be relieved by the return of spontaneous respiration [13, 43]. The maintenance of spontaneous ventilation if one is uncertain of the ability to intubate distal to the obstruction cannot be overemphasized.

Positioning changes may be necessary to alleviate airway obstruction after induction. Lateral, semierect, or prone positioning may be used [13, 44]. Occasionally, patients may require induction in a semierect or full sitting position [32]. Information regarding the patient's most comfortable breathing position will prove useful. Sufficient help in turning patients emergently should be immediately available.

Other techniques reported to manage airway obstruction include the use of direct laryngoscopy with the endotracheal tube in situ [14], percutaneous needle aspiration of the mass under LA preinduction [45], and bronchoscopic intubation with the aid of a laryngeal mask airway and intubation catheter [46].

In cases of severe respiratory or hemodynamic compromise after induction not responding to ventilation attempts including rigid bronchoscopy or positional changes, the surgeon may have to proceed quickly to an emergent sternotomy to lift the anterior mediastinal mass to alleviate its compressive effects. Severe hypoxia refractory to treatment with oxygen and ventilation may indicate cardiac compression from the mediastinal mass [47].

Ventilation

Ventilation after intubation depends on whether intubation is distal to the tracheobronchial obstruction. If that is certain, one can gradually take over the ventilation manually, and if this is well tolerated, positive pressure ventilation with or without short-acting muscle relaxants can be employed. If there is doubt about certainty of distal intubation or ability to ventilate, maintenance of spontaneous ventilation [30, 32] seems reasonable, with occasional assisted ventilation.

Other Issues

Specific issues pertaining to SVC obstruction include the possibility of excessive bleeding, the certainty of drug delivery to the effector site, and the possibility of airway swelling and stridor during emergence and after surgery. Large bore IV access established in the lower limbs [32], including possible central venous catheter in the femoral vein, immediate availability of blood, and postoperative ventilation may be necessary, especially if surgery is prolonged. Occasionally, the surgeons may need to clamp or resect the SVC.

Specific considerations for patients with myasthenia gravis will be dealt with in Chap. 15.

Cardiopulmonary bypass can be considered in situations when the ability to ventilate is unlikely or uncertain after induction, e.g., if the tumor compresses the distal third of the trachea, both mainstem bronchi or the carina. It can also be used when there is extensive tumor compression of the right heart or pulmonary artery, with significant risk of hemodynamic collapse after induction. Cardiopulmonary bypass, if planned, should always be established electively before induction [48, 49], as its use in an emergent rescue situation is unlikely to result in a favorable outcome [50]. Even a planned preinduction cardiopulmonary bypass can be difficult to execute [51]. It therefore requires advance planning and discussion with the surgical and perfusion teams. Soon et al. described in their case report the preinduction establishment of peripheral cardiopulmonary bypass for resection of a large thymoma causing severe tracheobronchial and superior vena cava compression. They instituted peripheral venoarterial bypass under local anesthesia with light sedation, with the arterial inflow via the common femoral artery, and the venous cannula directed up the femoral vein to the right atrium. After the establishment of cardiopulmonary bypass, the patient underwent inhalational induction and was intubated without relaxant. Only after decompression of the cystic tumor, when mechanical ventilation was certain, was the patient weaned from bypass [49].

Emergence and Recovery

Emergence and recovery may be complicated by airway obstruction, especially in diagnostic surgeries when the anterior mediastinal mass is not removed [1]. There is also risk of glottic edema and post-op stridor, in patients with SVC obstruction and prolonged surgeries. Complications involving the airway may be more common upon emergence and in the recovery period [52]. Extubation of the airway should only be done if the patient is completely awake and obeying commands, with full recovery of muscle strength. The use of short-acting anesthetic agents, narcotics, and muscle relaxants may be advantageous. Even with apparently successful extubation, the patient should be carefully monitored in the postanesthetic care unit, with the anesthesiologist prepared to emergently reintubate the patient, because any deterioration may be rapid.

Complications and Risk Factors

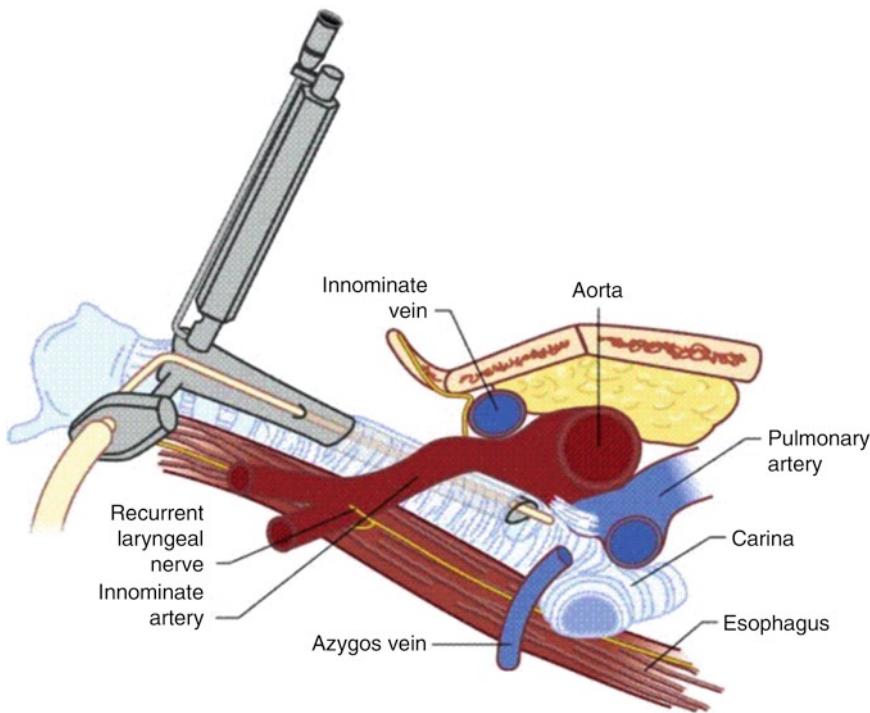
Complete airway obstruction and cardiovascular collapse are the most-feared complications that can occur during general anesthesia in patients with mediastinal masses [2, 3, 53]. Exacerbation of the compressive effects on the major airways [27, 43, 53] and cardiovascular structures (heart, pulmonary artery, superior vena cava) [53, 54] can result in profound hypoxemia and hypotension. They can occur unexpectedly at any time during anesthesia including preinduction, induction, positioning, surgery, emergence and extubation, or postoperatively in the PACU [1–3, 11, 27, 37, 43, 51]. The incidence of complications has been reported to be between 7 and 20%, mainly in the pediatric population [11, 27, 32, 55]. Bechard et al., in their adult series, reported the incidence of intraoperative cardiorespiratory and postoperative respiratory complications as 3.8 and 10.5%, respectively. The incidence of intraoperative airway obstruction was 0% in their series [52].

Various authors have attempted to identify risk factors predictive of perioperative cardiorespiratory complications. Studies were mainly performed in pediatric populations [11, 55–57]. In children, the anterior mediastinal masses associated with anesthetic problems are rapidly growing hematological malignancies [58]. King et al. proposed that respiratory symptoms were accurate indicators of significance of airway compression and risk of general anesthesia [55]. Hack et al. reported a poor correlation between clinical signs and size of tumor or tracheal compression on CT scan. They found stridor to be the only sign that predicted an anesthetic complication. Respiratory complications were found in patients with tracheal cross-sectional area less than 30% normal or less than 70% and associated with bronchial compression [29]. Azizkhan et al. reported a high rate of total airway obstruction during general anesthesia in children with tracheal compression greater than 50% [11]. Shamberger et al. concluded in their prospective study that general anesthesia could be given to children with tracheal area and peak expiratory flow rate greater than 50% of predicted [57]. Bechard et al. reported a high perioperative complication rate for adult patients with severe symptoms (stridor, orthopnea, cyanosis, jugular distension, SVC syndrome) in their univariate analysis. They found no perioperative complications in asymptomatic patients. Intraoperative complications were associated with pericardial effusion on CT scan. Postoperative respiratory complications were associated with tracheal compression of more than 50% on CT scan and combined obstructive and restrictive pattern on pulmonary function tests [52].

Anesthesia for Mediastinoscopy

Mediastinoscopy is a procedure widely used for staging of lung malignancy and for obtaining tissue for histological diagnosis of mediastinal masses. The two main approaches

FIG. 14.2. Diagram of a mediastinoscope in the pretracheal fascia along with relevant surrounding structures. Note the innominate artery immediately anterior to the mediastinoscope. The azygos vein drains into the superior vena cava, which has been omitted from the drawing because it would cover the location of the mediastinoscope (reprinted from Slinger and Campos [61] with permission).



are cervical mediastinoscopy and anterior mediastinoscopy. Far more common is cervical mediastinoscopy, where the scope is inserted beneath the manubrium and requires general anesthesia. Anterior mediastinoscopy is done via the second left interspace to inspect the lower left mediastinum. It can be done under local anesthesia [24].

Because the mediastinoscope is inserted near major blood vessels like the innominate artery and azygos vein, there is a risk of massive hemorrhage which can be life-threatening (Fig. 14.2). In a retrospective review, Park et al. reported the incidence of major hemorrhage as 0.4% [59]. The most frequently injured vessels were the azygos vein and the innominate and pulmonary arteries [59]. Other complications include compression of the trachea, compression of the innominate artery that can lead to cerebrovascular events and right upper limb ischemia, compression of the aorta leading to reflex bradycardia, pneumothorax, injury to the recurrent laryngeal nerve, and air embolism.

In addition to the anesthetic concerns for management of a mediastinal mass, the perioperative care of a patient undergoing mediastinoscopy has some unique considerations. There should be monitoring of the right upper limb pulse, either by pulse oximetry placed on a right finger or by invasive blood pressure established in the right upper limb. The noninvasive blood pressure can be measured from the left arm to ascertain systemic pressures. As there is a potential for massive hemorrhage, large-bore venous access is ideal. Lower limb venous access can be considered and availability of blood ascertained. General anesthesia with positive pressure ventilation via a single lumen endotracheal tube is usually used, with the patient in a supine position on a shoulder roll. The surgeon may have

to be alerted to excessive compression of the innominate artery (hence compression of the right common carotid) or the trachea by the mediastinoscope. Attention to the right arm arterial waveform and the peak inspiratory pressure is necessary.

In the event of bleeding, immediate preparations for resuscitation of massive hemorrhage should be undertaken, because patients can exsanguinate, while the surgeon tries to stop the bleeding. Initial control of the bleeding may be achieved through packing [59, 60]. There may be a necessity of conversion to a sternotomy or a thoracotomy [60], depending on the site of bleeding. Lung isolation, if necessary, may be done via a change to a double-lumen tube [60] but a bronchial blocker may be more useful in such extraneous circumstances, especially in a patient with a difficult airway. Lower limb venous access and invasive blood pressure monitoring should be established quickly, if not done previously. There should be immediate availability of blood and equipment for massive blood transfusion, including rapid transfusion devices, blood warmers, and possibly cell savers.

Patients can usually be extubated immediately after uncomplicated mediastinoscopy and may be discharged on the same day after a postoperative chest radiograph done to rule out the infrequent pneumothorax.

Summary

Anesthesia for patients with anterior mediastinal masses remains a challenge for the anesthesiologist. Attempting to identify patients at high risk for airway occlusion and

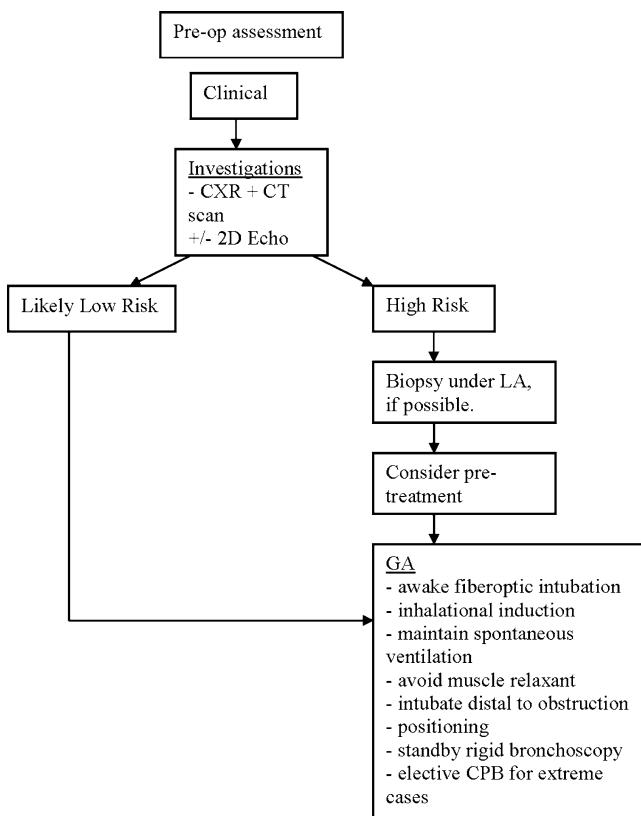


FIG. 14.3. Flow chart showing the anesthetic considerations for patients with anterior mediastinal masses.

cardiovascular collapse under general anesthesia continues to be difficult. Where possible, diagnostic procedures should be undertaken under local anesthesia. Understanding the relation of the mediastinal mass to vital structures, careful preoperative assessment of the patient, discussion with the surgeon, and careful planning and preparation for perioperative complications related to compression of the major airways and vascular structures are key to successful management. A careful anesthetic plan that is not irreversible is likely to result in a good outcome (see Figs. 14.3–14.6).

Clinical Case Discussion

A middle-aged obese woman with a history of asthma presents with a large anterior mediastinal mass for sternotomy and resection. She has vague symptoms of orthopnea, requiring two pillows to sleep. CT scan shows a 4 by 5-cm mass in the anterior mediastinum causing compression on the mid to distal trachea, with about 50% decrease in the cross-sectional area of the trachea in the narrowest portion.

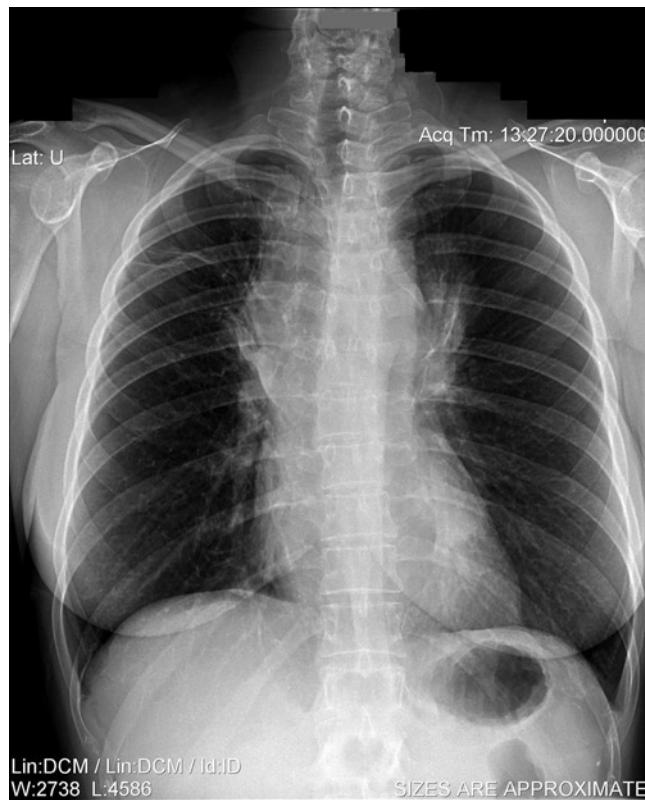


FIG. 14.4. Chest X-ray of a middle-aged woman with a recurrent anterior mediastinal mass and history of treated Hodgkin's lymphoma presenting for biopsy of the mass under GA. Recent percutaneous CT-guided biopsies were nondiagnostic. She was asymptomatic.

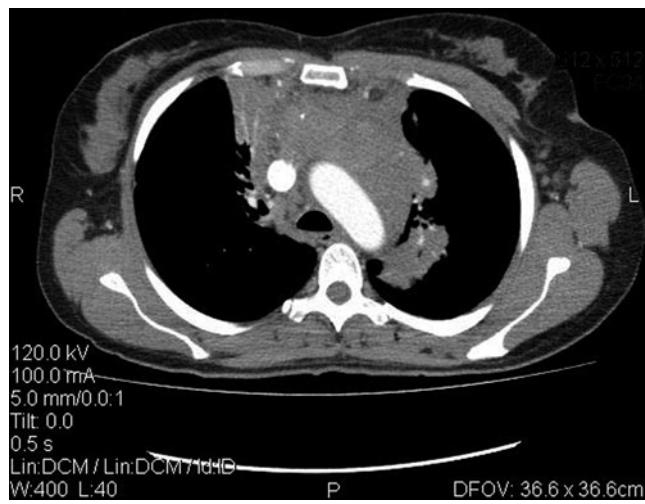


FIG. 14.5. CT scan of the same patient shows a large anterior mediastinal mass measuring 4.2 cm in its AP diameter. There is no obvious compression of the major airways or vascular structures. GA was uneventful and included a conventional intravenous induction with propofol and paralysis with succinylcholine for intubation. Biopsy eventually revealed a diagnosis of recurrent Hodgkin's lymphoma.

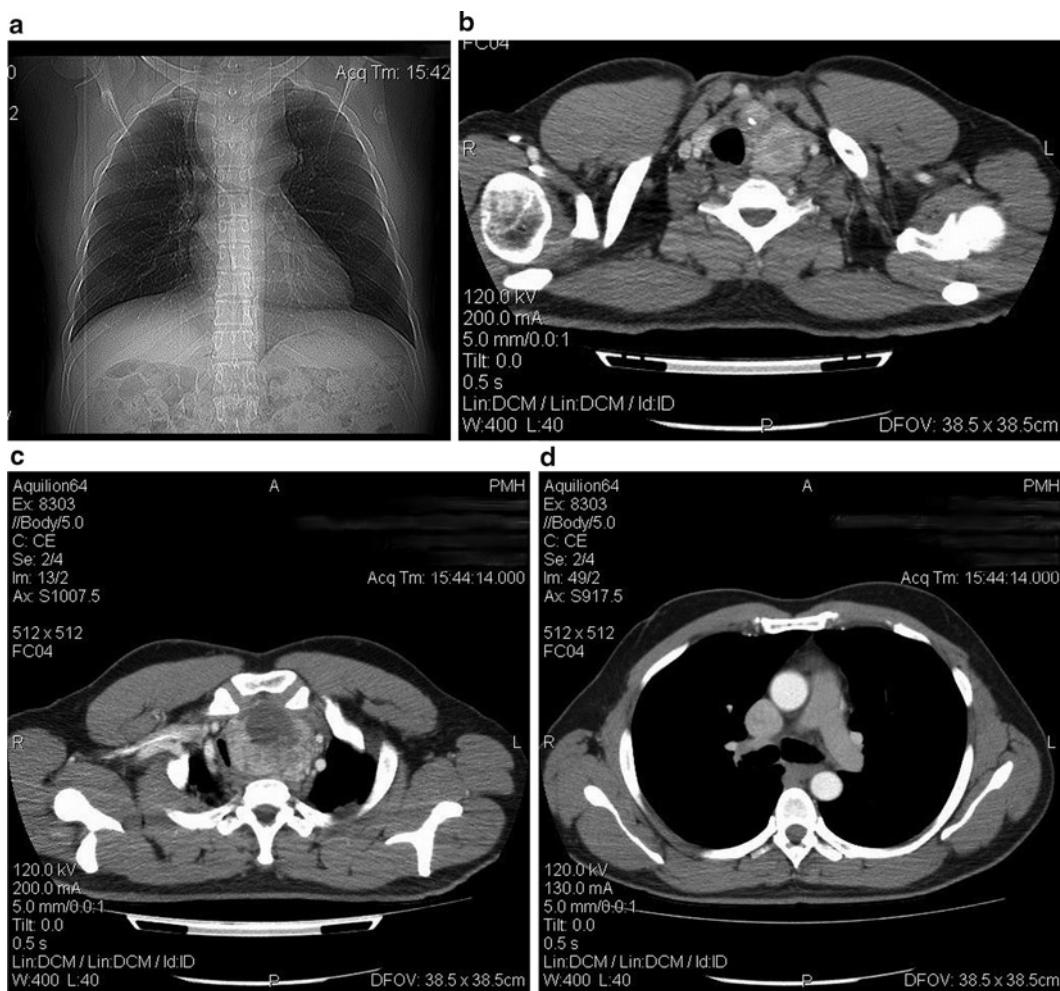


FIG. 14.6. (a) Chest X-ray of a 55-year-old female patient with mid-thoracic tracheal compression from an intrathoracic goiter. It shows trachea compression and deviation to the right. (b) CT scan of the same patient with mid-thoracic tracheal compression from an intrathoracic goiter. It shows the mediastinal mass pushing the trachea to the right. (c) CT scan of the patient with mid-thoracic tracheal compression from an intrathoracic goiter. It shows the trachea compressed to almost a slit by the mass. (d) CT scan of the patient with mid-thoracic tracheal compression from an intrathoracic goiter. It shows right and left main stem bronchi, relatively free from compressive effects. This patient was intubated distal to the stenosis awake.

Question 1

What are your options for induction of anesthesia?

Answer

This lady likely falls in the high risk category, in view of her symptoms and CT scan findings. The options include awake fiberoptic intubation and inhalational induction. The safest option is likely to be the former, which permits inspection of level of obstruction, the diameter of the airway, the least obstructed bronchus, and the passage of an endotracheal tube long enough to intubate distal to the obstruction. In this obese patient, an inhalational induction may be difficult, with partially obstructed respiration being a potential problem, and this technique may be difficult to abort midway.

Question 2

You successfully intubated the patient and gave a muscle relaxant. Soon after, the airway pressure rises to above 40 cm H₂O. Auscultation reveals bilateral rhonchi. She starts to desaturate rapidly. What do you suspect?

Answer

The diagnosis to exclude urgently is intubation proximal to the trachea obstruction. A quick check with the bronchoscope will help verify this. Pushing the endotracheal tube further in may result in improvement if that were indeed the problem, if it is possible to bypass the obstruction. Occasionally, endobronchial intubation may be necessary, but it may also cause hypoxemia, unless bilateral bronchi are intubated.

One should suspect that the obstruction is more distal than initially thought if one cannot bypass the obstruction, e.g., bilateral bronchi are obstructed as well. Paralysis and loss of spontaneous ventilation will exacerbate the problem of a proximal intubation. One should be very careful with muscle relaxants, using them only when ventilation is certain. If there are any doubts, avoid them.

The presence of rhonchi may suggest bronchospasm but that is usually a red herring. The most likely and urgent diagnosis to exclude is major airway obstruction. Rhonchi and high airway pressures may be the only clues to airway obstruction and should not automatically be attributed to peripheral bronchospasm in a patient with an anterior mediastinal mass.

The other important differential to consider in this patient is compression of major cardiovascular structures.

Question 3

The airway pressure continues to be high and the patient continues to desaturate despite your attempts at bronchoscopic adjustment of the endotracheal tube. The surgeons are scrubbing. What should you do?

Answer

Immediately alert the surgeon, who may want to do an urgent rigid bronchoscopy or proceed to immediate sternotomy to lift the mediastinal mass to relieve its compressive effects. Equipment should be on standby and immediately available. Changing the position of the patient may help. Endobronchial intubation may be attempted if the tube is long enough. Jet ventilation via a proximally intubated trachea may be considered.

The surgeons quickly performed a sternotomy and upon lifting the mass off the trachea and the right pulmonary artery, the airway pressure and saturation improved dramatically. That was the longest minute of your life!

References

1. Neuman GG, Weingarten AE, Abramowitz RM, Kushins LG, Abramson AL, Ladner W. The anesthetic management of the patient with an anterior mediastinal mass. *Anesthesiology*. 1984;60:144–7.
2. Levin H, Bursztein S, Heifetz M. Cardiac arrest in a child with an anterior mediastinal mass. *Anesth Analg*. 1985;64:1129–30.
3. Northrip DR, Bohman BK, Tsueda K. Total airway occlusion and superior vena cava syndrome in a child with an anterior mediastinal tumour. *Anesth Analg*. 1986;65:1079–82.
4. Victory RA, Casey W, Doherty P, Breathnach F. Cardiac and respiratory complications of mediastinal lymphomas. *Anaesth Intens Care*. 1993;21:366–9.
5. Hammer GB. Anaesthetic management for the child with a mediastinal mass. *Paediatr Anaesth*. 2004;14:95–7.
6. Warren WH. Anatomy of the mediastinum with special reference to surgical access. In: Pearson's thoracic and esophageal surgery. 3rd ed. Elsevier; 2009. Chapter 122. p. 1472.
7. DeCamp MM, Swanson SJ, Sugarbaker DJ. The mediastinum. In: Baue AE, Geha AS, Laks H, Hammond GL, Naunheim KS, editors. Glenn's thoracic and cardiovascular surgery. 6th ed. Appleton & Lange: Stamford; 1996. p. 643–63.
8. Yoneda KY, Louie S, Shelton DK. Mediastinal tumors. *Curr Opin Pulm Med*. 2001;7:226–33.
9. Dubashi B, Cyriac S, Tenali SG. Clinicopathological analysis and outcome of primary mediastinal malignancies – a report of 91 cases from a single institute. *Ann Thorac Med*. 2009;4:140–2.
10. Davis RDJ, Oldham HNJ, Sabiston DCJ. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. *Ann Thorac Surg*. 1987;44:229–37.
11. Azizkhan RG, Dudgeon DL, Buck JR, Colombani PM, Yaster M, Nichols D, et al. Life-threatening airway obstruction as a complication to the management of mediastinal masses in children. *J Pediatr Surg*. 1985;20:816–22.
12. John RE, Narang VP. A boy with an anterior mediastinal mass. *Anaesthesia*. 1988;43:864–6.
13. Bray RJ, Fernandes FJ. Mediastinal tumour causing airway obstruction in anaesthetized children. *Anaesthesia*. 1982;37: 571–5.
14. DeSoto H. Direct laryngoscopy as an aid to relieve airway obstruction in a patient with a mediastinal mass. *Anesthesiology*. 1987;67:116–7.
15. Froese AB, Bryan AC. Effects of anesthesia and paralysis on diaphragmatic mechanics in man. *Anesthesiology*. 1974;41:242–55.
16. Graeber GM, Shriver CD, Albus RA, Burton NA, Collins GJ, Lough FC, et al. The use of computed tomography in the evaluation of mediastinal masses. *J Thorac Cardiovasc Surg*. 1986;91:662–6.
17. Benumof JL. Anesthesia for thoracic surgery. 2nd ed. Philadelphia: Saunders; 1995. p. 570.
18. Prakash UB, Abel MD, Hubmayer RD. Mediastinal mass and tracheal obstruction during general anesthesia. *Mayo Clin Proc*. 1988;63:1004–11.
19. Miller RD, Hyatt RE. Obstructing lesions of the larynx and trachea: clinical and physiologic characteristics. *Mayo Clin Proc*. 1969;44:145–61.
20. Vander Els NJ, Sorhage F, Bach AM, Straus DJ, White DA. Abnormal flow volume loops in patients with intrathoracic Hodgkin's disease. *Chest*. 2000;117:1256–61.
21. Hnatiuk OW, Corcoran PC, Sierra A. Spirometry in surgery for anterior mediastinal masses. *Chest*. 2001;120:1152–6.
22. Kulkarni S, Kulkarni A, Roy D, Thakur MH. Percutaneous computed tomography guided-core biopsy for the diagnosis of mediastinal masses. *Ann Thorac Med*. 2008;3:13–7.
23. Dasan J, Littleford J, McRae K, Farine D, Winton T. Mediastinal tumor in a pregnant patient presenting as acute cardiorespiratory compromise. *Int J Obstet Anesth*. 2002;11:52–6.
24. Rendina EA, Venuta F, De Giacomo T, Ciccone AM, Moretti MS, Ibrahim M, et al. Biopsy of anterior mediastinal masses under local anesthesia. *Ann Thorac Surg*. 2002;74:1720–2.
25. Bacha EA, Chapelier AR, Macchiarini P, Fadel E, Darteville PG. Surgery for invasive primary mediastinal tumors. *Ann Thorac Surg*. 1998;66:234–9.
26. Szokol JW, Alspach D, Mehta MK, Parilla BV, Liptay MJ. Intermittent airway obstruction and superior vena cava syndrome in a patient with an undiagnosed mediastinal mass after cesarean delivery. *Anesth Analg*. 2003;97:883–4.

27. Piro A, Weiss D, Hellman S. Mediastinal Hodgkin's disease: a possible danger for intubation anesthesia. *Int J Radiat Oncol Biol Phys.* 1976;1:415–9.
28. Robie DK, Gursoy MS, Pokorny WJ. Mediastinal tumors – airway obstruction and management. *Semin Pediatr Surg.* 1994;3: 259–66.
29. Hack HA, Wright NB, Wynn RF. The anaesthetic management of children with anterior mediastinal masses. *Anaesthesia.* 2008;63:837–46.
30. Sibert KS, Biondi JW, Hirsch NP. Spontaneous respiration during thoracotomy in a patient with a mediastinal mass. *Anesth Analg.* 1987;66:904–7.
31. Turoff RD, Gomez GA, Berjian R, Park JJ, Priore RL, Lawrence DD, et al. Postoperative respiratory complications in patients with Hodgkin's disease: relationship to the size of the mediastinal tumor. *Eur J Cancer Clin Oncol.* 1985;21:1043–6.
32. Ferrari LR, Bedford RF. General anesthesia prior to treatment of anterior mediastinal masses in pediatric cancer patients. *Anesthesiology.* 1990;72:991–5.
33. Pullerits J, Holzman R. Anaesthesia for patients with mediastinal masses. *Can J Anaesth.* 1989;36:681–8.
34. Greengrass R. Anaesthesia and mediastinal masses. *Can J Anaesth.* 1990;37:596–7.
35. Tinker DT, Crane DL. Safety of anesthesia for patients with anterior mediastinal masses I. *Anesthesiology.* 1990;73:1060.
36. Zornow MH, Benumof JL. Safety of anesthesia for patients with anterior mediastinal masses II. *Anesthesiology.* 1990;73:1061.
37. Mackie AM, Watson CB. Anaesthesia and mediastinal masses. *Anaesthesia.* 1984;39:899–903.
38. Goh MH, Liu XY, Goh YS. Anterior mediastinal masses: an anaesthetic challenge. *Anaesthesia.* 1999;54:670–82.
39. Narang S, Harte BH, Body SC. Anesthesia for patients with a mediastinal mass. *Anesthesiol Clin North Am.* 2001;19: 559–79.
40. Shamberger RC. Preanesthetic evaluation of children with anterior mediastinal masses. *Semin Pediatr Surg.* 1999;8:61–8.
41. Frawley G, Low J, Brown TCK. Anaesthesia for an anterior mediastinal mass with ketamine and midazolam infusion. *Anaesth Intens Care.* 1995;23:610–2.
42. Stewart AS, Smythe WR, Aukburg S, Kaiser LR, Fox KR, Bavaria JE. Severe acute extrinsic airway compression by mediastinal tumor successfully managed with extracorporeal membrane oxygenation. *ASAIO J.* 1998;44:219–21.
43. Bittar D. Respiratory obstruction associated with induction of general anesthesia in a patient with mediastinal Hodgkin's disease. *Anesth Analg.* 1975;54:399–403.
44. O'Leary HT, Tracey JA. Mediastinal tumours causing airway obstruction: a case in an adult. *Anaesthesia.* 1983;38:67.
45. Flaherty S, Grishkin BA. Airway obstruction by anterior mediastinal mass. Successful management by percutaneous aspiration. *Chest.* 1994;106:947–8.
46. Capdeville M. The management of a patient with tracheal compression undergoing combined resection of an anterior mediastinal mass and aortic valve replacement with coronary artery bypass graft surgery: utility of the laryngeal mask airway and an Aintree intubation catheter. *J Cardiothorac Vasc Anesth.* 2007;21:259–61.
47. Russell JC, Lowry KG. Presentation of non-Hodgkin's lymphoma as acute hypoxia caused by right ventricular compression. *Anesth Analg.* 2003;96:1768–71.
48. Tempe DK, Arya R, Dubey S, Khanna S, Tomar AS, Grover V, et al. Mediastinal mass resection: femorofemoral cardiopulmonary bypass before the induction of anaesthesia in the management of airway obstruction. *J Cardiothorac Vasc Anesth.* 2001;15:233–6.
49. Soon JL, Poopalalingam R, Lim CH, Koong HN, Agasthian T. Peripheral cardiopulmonary bypass-assisted thymoma resection. *J Cardiothorac Vasc Anesth.* 2007;21:867–9.
50. Turkoz A, Gulcan O, Tercan F. Hemodynamic collapse caused by a large unruptured aneurysm of the ascending aorta in an 18 year old. *Anesth Analg.* 2006;102:1040–2.
51. Asai T. Emergency cardiopulmonary bypass in a patient with a mediastinal mass. *Anaesthesia.* 2007;62:859–60.
52. Bechard P, Letourneau L, Lacasse Y, Cote D, Bussieres JS. Perioperative cardiorespiratory complications in adults with mediastinal mass. *Anesthesiology.* 2004;100:826–34.
53. Keon TP. Death on induction of anesthesia for cervical node biopsy. *Anesthesiology.* 1981;55:471–2.
54. Goodman R. Superior vena cava syndrome. Clinical management. *JAMA.* 1975;231:58–61.
55. King DR, Patrick LE, Ginn-Pease ME, McCoy KS, Klopfenstein K. Pulmonary function is compromised in children with mediastinal lymphoma. *J Pediatr Surg.* 1997;32:294–9.
56. Shamberger RC, Holzman RS, Griscom NT, Tarbell NJ, Weinstein HJ. CT quantification of tracheal cross-sectional area as a guide to the surgical and anesthetic management of children with anterior mediastinal masses. *J Pediatr Surg.* 1991;26: 138–42.
57. Shamberger RC, Holzman RS, Griscom NT, Tarbell NJ, Weinstein HJ, Wohl ME. Prospective evaluation by computed tomography and pulmonary function tests of children with mediastinal masses. *Surgery.* 1995;118:468–71.
58. King RM, Telander RL, Smithson WA, Banks PM, Han MT. Primary mediastinal tumors in children. *J Pediatr Surg.* 1982;17:512–20.
59. Park BJ, Flores R, Downey RJ, Bains MS, Rusch VW. Management of major hemorrhage during mediastinoscopy. *J Thorac Cardiovasc Surg.* 2003;126:726–31.
60. Lohser J, Donington JS, Mitchell JD, Brodsky JB, Raman J, Slinger P. Case 5 – 2005: anesthetic management of major hemorrhage during mediastinoscopy. *J Cardiothorac Vasc Anesth.* 2005;19:678–83.
61. Slinger PD, Campos JH. Anesthesia for thoracic surgery. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. *Miller's anesthesia.* 7th ed. Amsterdam: Elsevier; 2009. p. 1856.

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Key Points

- Indications for thymectomy typically include thymic mass or nonthymomatous myasthenia gravis (MG).
- Considerations for a patient with a thymic mass include potential for invasion or compression of cardiopulmonary structures causing life-threatening compromise particularly at induction of general anesthesia.
- Thymectomy for MG is never an emergency procedure and should not proceed without preoperative optimization by a multidisciplinary team specializing in the care of myasthenic patients.
- Anesthetic considerations for a patient with MG focus on preventing an exacerbation and minimizing the effect of surgical pain and residual anesthetics on postoperative respiratory function.
- Muscle relaxants and their reversal agents should be avoided in patients with MG whenever possible. Other principles include the use of short-acting agents, use of regional anesthesia for opioid-sparing effects, and proper perioperative management of anticholinesterases.
- Despite repeated efforts to determine what clinical features predict the need for postoperative ventilation, no criteria have been proven to be universally applicable in the myasthenic population.
- Many thoracic malignancies have commonly associated paraneoplastic syndromes with important implications for the anaesthesiologist.
- The most common extra-intestinal location of carcinoid tumors is the lungs; however, unlike their gastrointestinal counterparts, bronchial carcinoids are rarely secretory.

- Carcinoid syndrome must be optimized with at least 24 h of preoperative octreotide to minimize the life-threatening cardio-pulmonary instability that can occur during a carcinoid crisis.
- Advanced carcinoid disease is associated with fibrosis which can lead to pulmonary hypertension or significant valvulopathy with progressive, severe, right-sided heart failure. For these reasons, patients presenting with carcinoid syndrome must have a preoperative echocardiogram.

Introduction

The thymus gland is situated in the anterior mediastinum; protected by the sternum and ribcage, it is nestled amid vital cardiopulmonary structures. Its function and reason for involution are unknown, yet it gives rise to a range of pathology with which the thoracic anaesthesiologist must be familiar. The intimate relationship between the thymus gland and myasthenia gravis (MG) is well-established. The implications of acquired myasthenia are essential material for the anaesthesiologist, and therefore, much of this chapter is devoted to this important neuromuscular condition. Other paraneoplastic and paraendocrine syndromes with important perioperative implications include the carcinoid syndrome, Lambert–Eaton syndrome (LES), and other endocrine derangements commonly associated with malignancies. The final part of this chapter deals with these.

Thymic Surgery

Common indications for thymectomy include MG and the presence of thymic masses. Thymectomy for MG is covered in the following section. Here, the common masses of the

thymus are briefly reviewed along with general anesthetic considerations. As an anterior mediastinal structure, the reader is also referred to Chap. 14 which addresses anterior mediastinal masses and the potential for compressive effects.

The most common tumor of the thymus and the anterior mediastinum is thymoma. Thymoma may be invasive or non-invasive and 40% have associated paraneoplastic syndromes [1]. The most commonly associated paraneoplastic syndrome is MG (30%) but systemic lupus erythematosus, Cushing's syndrome, syndrome of inappropriate diuretic hormone secretion, and pure red cell aplasia may also be associated [2].

Thymic carcinoma are much more rare than thymoma and in contrast, they are always invasive and often present with symptoms reflective of their aggressive nature [3]. Paraneoplastic syndromes are possible but are much less common [4].

Thymic carcinoid is the most common member of the rare group of thymic neuroendocrine neoplasms. It is a potentially secretory tumor, commonly manifesting Cushing's syndrome rather than the typical carcinoid syndrome [5]. At least 15% of thymic carcinoids present as part of multiple endocrine neoplasia (MEN-1) syndrome [1]. Surgery plays an important role in the management of thymic masses. Removal of all thymic tissue and perithymic fat through a median sternotomy is the current standard of care [6, 7].

The anesthesia considerations for nonmyasthenia thymic surgery are similar to those for any malignancy. Due to the location in the anterior mediastinum the anesthetist must maintain suspicion of compression of the major cardiopulmonary structures [8–10]. A history of cough, chest discomfort, dyspnea, palpitations, and syncope should be sought including any change associated with assuming the supine position. Symptoms may also occur due to paraneoplastic and paraendocrine syndromes, as detailed later in this chapter. Clinicians should screen for MG by inquiring about blurring vision, difficulty swallowing or difficulty with speech. Invasive thymoma and thymic carcinoma tend to invade surrounding structures including major airways, pericardium, and great vessels therefore imaging should be reviewed and resection of major structures discussed with the surgeon preoperatively [11]. A history of any preceding treatment should also be sought. Radiation to the chest can result in pulmonary fibrosis, coronary artery disease, and pericarditis [12] and many chemotherapeutic agents have known implications for perioperative management. Cisplatin, a potential nephrotoxin, is one of the most common chemotherapeutic drugs used in the treatment of thymoma; doxorubicin, vincristine, and others may also be used [13, 14].

Myasthenia Gravis

First described in the seventeenth century, MG did not become a recognized entity until over 200 years later when Dr. Friedrich Jolly titled the syndrome, “myasthenia gravis

pseudoparalytica” [15, 16]. At that time, MG almost uniformly caused death by respiratory failure within 1–2 years of illness. With a prevalence of 1:17,000 [17] and an established role for surgery in its management, the anesthesiologist must know how to optimize and safely manage these patients perioperatively.

Pathophysiology

MG is an autoimmune disease due to antibody-mediated destruction of nicotinic acetylcholine receptors [18]. As a result, the neuromuscular junctions (NMJs) of all muscles, even clinically unaffected muscles, have a reduced number of acetylcholine receptors [19, 20]. In addition to a reduced number of acetylcholine receptors, other abnormalities of the NMJ include a reduced number and depth of the junctional folds in the postsynaptic membrane [21]. Auto-antibodies are detectable in most cases and the 10–20% of patients once considered “sero-negative” are now known to possess antibodies as well.

Patients present with fluctuating skeletal muscle weakness which is made worse by activity and improves with rest. The reduction in postsynaptic acetylcholine receptors results in generation of fewer motor end-plate potentials therefore fewer muscle fibers stimulated to contract. With repeated or continued stimulation, even less motor end-plate potentials reach threshold, and weakness becomes more pronounced.

The cause of the immune reaction leading to MG is unknown. A very strong link exists between MG and thymic pathology. Most patients with MG exhibit thymic abnormalities which can range from hyperplasia (70–80%) to the presence of thymoma (10–15%) and 15% of patients with thymoma have MG. Furthermore, removal of the thymus results in clinical improvement in the majority of cases of MG [20, 22, 23].

MG is often associated with other conditions which share an underlying autoimmune tendency [17]. Diabetes and thyroid disorders (hyperthyroid or hypothyroid) are present in 5–6% and 1–2% have rheumatoid arthritis. Systemic lupus erythematosus, leukemia, scleroderma, and polymyositis have also been found in higher numbers in the myasthenic population than in the general population [24].

Presentation

The majority of patients initially present due to diplopia (leading to blurring vision) or ptosis. Other presentations include difficulty swallowing or speaking due to bulbar dysfunction, dyspnea due to respiratory muscle compromise, or weakness of the neck or limbs. Symptoms always worsen with the use of the affected muscles and strength returns with rest [16, 17].

In addition to the neuromuscular manifestations and associated conditions mentioned above, MG can also affect the heart directly causing palpitations and dyspnea. Common cardiac manifestations include mild hypertension, first-degree atrioventricular block, atrial fibrillation, and myocarditis. Diastolic dysfunction has also been noted [25–27].

Diagnosis

Since 1952, the first line diagnostic test for MG remains the “Tensilon Test” [28]. As an anti-cholinesterase of rapid onset (30 s) and offset (5 min), edrophonium (tensilon), is ideal for diagnostic testing. The inhibition of acetylcholine breakdown allows acetylcholine to accumulate and stimulate the reduced number of postjunctional receptors. Intravenous edrophonium is administered and muscle performance is assessed within 30–90 s. Clear improvement in the affected muscles, as measured qualitatively and quantitatively, is diagnostic of MG [20, 24]. Other tests such as repetitive nerve stimulation and antibody immunoassays are also available but are not first-line diagnostic tests.

Classification

In 1971, Dr. Osserman based a classification scheme on the observation of over 1,200 patients at the Myasthenia Gravis Clinic in New York [24]. In its modified form, this continues to be of use today (see Table 15.1). Patients are placed into a grade based on their weakest muscle group. More recently, a task force put together by the Myasthenia Gravis Foundation of America (MGFA) developed a clinical classification scheme to facilitate standardization of reporting (see Table 15.2) [30].

Medical Management

Pyridostigmine (Mestinon) is the anticholinesterase of choice for management of MG. Others are available for oral use, however, the effectiveness, kinetics, and tolerability of pyridostigmine is the most favorable [31]. Side effects, usually uncommon or mild, include diarrhea, bronchorrhea, and abdominal cramping.

TABLE 15.1. Modified Osserman grades.

Type I	Disease localized to ocular muscles Tends not to progress if remains confined to ocular muscles for first 2 years
Type IIA	Mild generalized myasthenia Slowly progressive often from ocular muscles to skeletal and bulbar muscles however, spares muscles of respiration Good response to drug therapy and low mortality
Type IIB	Moderate generalized myasthenia Gradual onset, usually ocular, progressing to more generalized bulbar and skeletal muscle involvement Respiratory muscles are not involved More bulbar symptoms than IIA Less responsive to medical therapy than IIA
Type III	Severe disease Progression may be gradual or sudden deterioration Poor response to drug therapy High mortality
Type IV	Myasthenic Crisis with respiratory failure Require intubation

Based on data from refs. [24, 29]

After an oral dose of pyridostigmine, an effect may be seen as early as 30 min later and the peak effect is reached 1 or 2 h later. The duration of action is usually between 3 and 6 h. The nonsustained release formulation can be crushed and given via nasogastric tube. If required, pyridostigmine can also be given intravenously with an oral to intravenous ratio of 30:1.

There is great inter-individual variability in the kinetics of oral pyridostigmine therefore the dose and frequency are titrated to reach optimum effect for each individual [31, 32]. The symptomatic control provided by anticholinesterases is often incomplete so most patients find themselves on additional medication in the form of immunosuppression.

Corticosteroids are commonly used to treat MG; however, the considerable side effect profile (see Table 15.3) of long-term corticosteroids makes them undesirable as an immunosuppressant. Once a patient has achieved remission, corticosteroids are usually tapered to their lowest effective dose. Frequently, corticosteroids are helpful to gain more control of the disease process while other immunosuppressants are being initiated [33].

TABLE 15.2. MGFA clinical classification.

Class	Description	Sub-classification (where applicable)
I	Isolated ocular weakness	No subclassification
II	Mild weakness of extra-ocular muscles	Class II and III are further subclassified: (a) Predominantly affecting limb, axial muscles, or both
III	Moderate weakness of extra-ocular muscles	(b) Predominantly affecting oropharyngeal, respiratory muscles, or both
IV	Severe weakness of extra-ocular muscles	IV(b) Use of feeding tube without intubation
V	Intubation	No subclassification

Adapted from ref. [30]

TABLE 15.3. Adverse effects of corticosteroids.

Gastrointestinal
• Dyspepsia
• Peptic ulcers
Body habitus
• Truncal obesity
Skin and musculoskeletal
• Acne
• Easy bruising
• Delayed wound healing
• Aseptic necrosis of femoral head
• Osteoporosis
Metabolic, fluid and electrolyte
• Hypertension
• Peripheral edema
• Hypokalemia
• Hyperglycemia/glucose intolerance
• Adrenal suppression
Muscle
• Myopathy
Behavioral
• Anxiety
• Psychosis

Azathioprine (“Imuran”) is one such alternative immunosuppressant which may take months to have an effect. A maximal benefit may take up to 24 months however its use allows corticosteroids to be minimized [31]. Adverse effects include bone marrow suppression, hepatotoxicity (usually mild and reversible), and gastrointestinal upset.

Cyclosporine is a potent immunosuppressant with onset much sooner than azathioprine. Its use is limited by the greater risks of toxicity. Common and severe adverse effects include hypertension, nephrotoxicity, hepatotoxicity, and bone marrow suppression. Levels must be monitored regularly [31, 33].

First reported in 1976 [34], the role of plasmapheresis for the treatment of MG has grown substantially. Treatments occur over 1–2 weeks and consist of three to five exchanges of plasma via a temporarily placed dialysis catheter. Each treatment removes 1–3 L. There is a reduction in acetylcholine receptor antibody titers in patients who have measurable antibodies. Benefits are usually seen after one or two exchanges and, once a course is completed, the improvement can last for 2 weeks to 2 months. Indications for treatment include bulbar symptoms, myasthenic crisis, or preoperative optimization [27].

Intravenous immunoglobulin (IVIG) represents a similar immune mediating therapy for MG. Its role is not as extensively studied as plasmapheresis and a recent Cochrane review based on six randomized control trials found limited evidence for its use in chronic MG [35]. However, IVIG may still be used when plasmapheresis cannot be applied [36]. As a blood product pooled from a large volume of donor plasma, it carries with it the risks inherent to any blood product. The dose is given intravenously over 2–5 days and adverse reactions are mild and tolerable (fever, nausea, headache). Benefit is seen within 4 days and peaks by 2 weeks; it may last 40–100 days. The mechanism of action remains unknown.

Surgical Management

In 1939, the first thymectomy was performed by Dr. Blalock and resulted in remission of MG [37]. Dr. Blalock followed this success with a series of thymectomies with similarly positive results [38, 39]. Today, thymectomy remains an important part of the management of MG although there remains controversy regarding its indications, timing and preferred surgical approach [40–45].

The clearest indication for thymectomy remains the presence of a thymoma. The other generally accepted indication for thymectomy is adults with generalized myasthenia gravis [31, 32].

Remission does not immediately follow removal of the thymus gland. It may take months to years for remission or significant improvement in the disease to occur. By 5 years, 34–46% of patients have complete remission and another 33–40% are significantly improved [31].

The preferred surgical approach to thymectomy is controversial. Possible approaches include transsternal, transcervical, or thoracoscopic as well as other less conventional approaches.

In the presence of thymoma, a transsternal approach remains the standard of care [46]. For patients with nonthymomatous MG, the argument in support of transsternal incision is that removal of as much thymic tissue as possible gives better long-term disease remission rates [40, 43]. However, proponents of the transcervical thymectomy have shown that adequate tissue can be removed to permit good long-term results while postoperative morbidity is reduced, allowing discharge from the hospital on the same day [41]. The advent of minimally invasive techniques has led to thoracoscopic thymectomy. Results have similarly been favorable in terms of disease remission, low morbidity and short hospital stays [42, 44]. The debate over which surgical approach is optimal continues and the anesthesiologist will therefore encounter more than one.

Myasthenic vs. Cholinergic Crisis

A myasthenic crisis refers to rapidly deteriorating strength which threatens the life of the patient. The most common causes of crisis are infection, surgery, and drugs (see Table 15.4); however, in many cases, no underlying precipitant can be found.

Patients with myasthenic crisis will be in respiratory failure due to weakness of the diaphragm and other muscles of respiration. Management requires intubation and admission to an intensive care unit for respiratory care [48]. Correctable causes should be sought and treated. Frequently patients will require plasmapheresis or IVIG to manage their exacerbation.

In contrast to a myasthenic crisis, a cholinergic crisis is caused by too much acetylcholine at the cholinergic receptors. It is most often caused by a relative overdose of anticholinesterase. This syndrome has become uncommon with present day management because the use of immunosuppressants has meant that lower doses of anticholinesterases are used [47]. The high levels of acetylcholine at all cholinergic receptors have multi-system effects. At the NMJ, it creates an endogenous depolarizing type of phenomenon causing fasciculations and muscle weakness [48]. The respiratory distress due to muscle weakness may be further compounded by bronchorrhea. Other manifestations are attributable to muscarinic stimulation (Table 15.5).

TABLE 15.4. Precipitants of myasthenic crisis.

Stress
Surgery
Infection
Drugs
<ul style="list-style-type: none"> • Aminoglycosides • Quinolones • Macrolides • Beta blockers • Calcium-channel blockers • Magnesium salts • Iodinated contrast agents • Phenytoin • Procainamide

Based on data from ref. [47]

TABLE 15.5. Manifestations of cholinergic crisis.
Motor: fasciculations, weakness
Cardiac: bradycardia
Respiratory: bronchorrhea
Ocular: miosis
Gastrointestinal: salivation, nausea, vomiting, colic, diarrhea
General: pallor, diaphoresis

TABLE 15.6. Leventhal criteria.

- Disease duration >6 years
- Pyridostigmine dose >750 mg/day
- Preoperative vital capacity <2.9 L
- Presence of other chronic respiratory disease

Based on data from ref. [49]

Differentiating a cholinergic vs. myasthenic crisis can be difficult as both present with weakness and respiratory distress. In addition to a history of recent events, pupil size, muscarinic signs, and tensilon test may be helpful. The pupils are constricted in a cholinergic crisis and dilated in a myasthenic crisis (due to sympathetic activation). Treatment includes intubation, antimuscarinics, and supportive care.

Anesthetic Considerations

The anesthesiologist will be confronted with myasthenic patients coming for thymectomy as well as those coming for surgery unrelated to their disease. Whenever possible, surgery should never be undertaken without preoperative stabilization and optimization of MG.

Anesthetic considerations include minimizing the risk of a myasthenic crisis and facilitating sustained extubation at the end of a general anesthetic. If a thymectomy is planned, then considerations of thymoma and an anterior mediastinal mass may also apply (see earlier).

Preoperatively, it is important to ask about the duration of disease and its severity, particularly with respect to ocular, bulbar, respiratory, and generalized symptoms. Many attempts have been made to delineate preoperative characteristics which predict the need for postoperative ventilation. The Leventhal criteria are often cited for this purpose [49] and are based on a retrospective review of 24 patients who underwent transsternal thymectomy (see Table 15.6). The criteria have been evaluated in other settings and have been found inaccurate in predicting the need for postoperative ventilation in patients undergoing other types of thymectomy as well as nonthymectomy surgery [50, 51]. Despite continued attempts to develop a model predictive of the need for postoperative ventilation, no such model has been consistently reliable. Anesthesiologists may use a series of preoperative factors examined in the literature which have been suggested to be predictive in various settings (see Table 15.7).

Patients should be questioned for any cardiac symptoms of palpitations, syncope, dyspnea, and any manifestations of congestive heart failure. A history of associated autoimmune con-

TABLE 15.7. Prediction of myasthenia gravis patients at high risk of prolonged postoperative ventilator support.

- Advanced disease
- Myasthenia gravis foundation class II or higher
- Myasthenia gravis >6 years
- History of steroids requirements for myasthenia gravis
- History of myasthenia gravis-induced respiratory insufficiency
- Vital capacity <2.9 L
- Pyridostigmine dose >750 mg/day
- Maximum expiratory force <40–50 cm H₂O

Based on data from refs. [27, 49, 52–54]

TABLE 15.8. Suggested preoperative investigations for the patient with myasthenia gravis.

Complete blood count	May have pernicious anemia, red cell aplasia, bone marrow suppression from immunosuppressants
Electrolytes	Optimized for neuromuscular function
Creatinine, liver function	As required based on use of immunosuppressants
TSH	Commonly have thyroid dysfunction
Chest X-ray	Rule out thymoma/mediastinal mass, pneumonia (particular aspiration if bulbar symptoms)
ECG	Arrhythmias, atrial fibrillation
Echo	If signs or symptoms of cardiac involvement
Pulmonary function tests	Useful to compare to previous for baseline

ditions, particularly thyroid dysfunction, should be sought. In order to plan perioperative medical management, a detailed history of current medications should be noted on the chart. Use of corticosteroids is usually tapered or discontinued preoperatively where possible but ongoing use may necessitate a stress dose of steroids preoperatively. The use of other immunosuppressants should also prompt a search for signs of toxicity or adverse effects. Table 15.8 lists suggested preoperative investigations.

Preoperative optimization should be undertaken in cooperation with a neurologist familiar with the care of patients with myasthenia. Plasmapheresis or IVIG may be arranged in order to reduce the chances of perioperative respiratory failure. As these treatments are not without adverse effects, their routine use may expose patients to unnecessary risk [55]. In general, patients with advanced disease, bulbar symptoms, or poor pulmonary function receive these immune modulating therapies [27, 56]. It should be noted that preoperative plasmapheresis depletes plasma cholinesterase so the duration of some anesthetics (i.e., succinylcholine, mivacurium) will be prolonged [29].

There are different approaches to peri-operative dosing of anticholinesterases. Some advocate the complete omission of anticholinesterase medications on the day of surgery in order to reduce the need for muscle relaxants [57]. Anticholinesterases may be given intraoperatively near the end of the procedure to facilitate extubation with this approach. See Table 15.9 for useful conversion factors of anticholinesterase drugs. Another approach is to give half the usual morning dose for patients with grade I or II disease and the full dose for more severe cases [59]. Still others advocate giving patients their full dose at their usual schedule [60].

TABLE 15.9. Conversion between anticholinesterases for management of myasthenia gravis.

Drug and formulation	Dose equivalent	Onset	Time to maximum response
Pyridostigmine oral (mestinon)	60 mg oral	40 min	1 h
Neostigmine oral (prostigmin)	15 mg oral	1 h	1.5 h
Neostigmine IM	1.5 mg	30 min	1 h
Neostigmine IV	0.5 mg	Immediate	20 min

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The approach followed at our institution, as well as others, is to give patients their usual dose of pyridostigmine preoperatively. Ideally, the patient is able to delay their morning dose until immediately preoperatively when it is given with a sip of water. Patients are scheduled as early in the day as possible to facilitate this approach. The goal is optimal strength at the time of extubation. It is generally agreed that myasthenics should not receive any preoperative sedation or anxiolytics. Monitors and invasive lines are dictated by the individual patient and planned surgery however, if neuromuscular blocking drugs are used, the use of nerve monitoring is essential.

Myasthenic patients are exquisitely sensitive to all nondepolarizing muscle relaxants (NDMR) [61–63]. The underlying muscle weakness due to the disease combined with the muscle relaxing properties of intravenous and volatile anesthetics often makes the use of muscle relaxants unnecessary. However, circumstances may arise when paralysis becomes necessary. For intermediate-acting neuromuscular blocking agents a dose reduction to one-fifth the usual is recommended. Long-acting neuromuscular blockade, such as with pancuronium, should be avoided [64, 65]. The use of paralytic agents should be combined with close nerve monitoring. Patients who have received their pyridostigmine preoperatively may have a prolonged duration of action of mivacurium due to the interaction with plasma cholinesterase [66].

The reversal of neuromuscular blockade is another area of controversy. The safest recommendation is to chose a minimal dose of a short-acting NDMR and allow the effect to terminate spontaneously [60]. Postoperatively, if a patient appears weak and in respiratory distress, differentiating between insufficient reversal and cholinergic crisis is very difficult. If such a situation is encountered, supportive care with appropriate ventilation is recommended until strength is regained.

In contrast to the response to NDMR, myasthenic patients show resistance to succinylcholine due to the loss of nicotinic receptors [67, 68]. Eisenkraft et al. have demonstrated that the ED50 is 2.0 times normal and recommend using a dose of 1.5–2.0 mg/kg if rapid sequence induction conditions are required [67]. The onset of the depolarizing block may take longer than expected [60]. Myasthenics are also more likely to develop a phase II block, particularly with repeated doses [69] and the duration of action may be prolonged if cholinesterase inhibitors have been taken that day.

Volatile anesthetics (halothane and particularly sevoflurane and isoflurane) have potent muscle relaxation effects in normal patients and have been shown to reduce neuromuscular transmission by close to 50% [70–72]. The dose of volatile required to achieve this depth may lead to delayed emergence. To minimize inhalational agents, they have been combined with regional anesthesia [73] or remifentanil infusion [73]. Desflurane's lower blood:gas partition coefficient has a theoretical advantage and has been used with good results [74, 75].

The use of total intravenous anesthesia (TIVA) for patients with MG seems to have grown, particularly with the widespread use of remifentanil [74, 76, 77]. Propofol, etomidate, and ketamine have also been used uneventfully and effects on neuromuscular transmission are minimal [78]. Opioids, while not directly suppressing neuromuscular function, should be minimized because of the central respiratory depression. For pain management perioperatively, consideration should be given to opioid-sparing techniques such as regional anesthesia or multimodal analgesia plans. Opioids with a shorter duration of action should be favored.

The use of regional anesthesia for myasthenics has many advantages; however, possible drug interactions must be kept in mind [79]. Local anesthetics (ester and amide) have some inhibitory effect on neuromuscular transmission and this can be potentiated further in the presence of NDMR [80]. Ester local anesthetics have an additional interaction because of their metabolism by plasma cholinesterase. The presence of anticholinesterase medication may prolong the ester duration of action as an inhibitory influence on neuromuscular transmission. If regional anesthesia is used, it is recommended to reduce the dose of local anesthetics [32, 64].

The place of thoracic epidural anesthesia (TEA) in the perioperative management of MG has changed dramatically. Traditionally, concern over blockade of intercostal muscles causing respiratory distress precluded the use of TEA [60]. Many examples now exist of the successful use of TEA intraoperatively as well as postoperatively [77, 81–83]. The benefits of excellent analgesia, muscle relaxation, and opioid sparing have translated into earlier extubation and a reduced need for postoperative ventilator support [77, 82]. Intrathecal opioids have similarly proven beneficial in terms of analgesia and optimizing respiratory function postoperatively [84, 85].

Clearly the perioperative management of patients with MG coming for any type of surgery requires a team of experts in neurology, surgery, and anesthesia. No particular anesthetic technique has proven superior for MG. The individualization of a perioperative plan with the principles presented here is suggested.

Paraendocrine and Paraneoplastic Syndromes

Paraendocrine and paraneoplastic syndromes must be kept in mind when patients present with malignancy. Table 15.10 contains the most common paraneoplastic syndromes that may be

TABLE 15.10. Common paraneoplastic syndromes.

	Humoral hypercalcemia	SIADH	Cushing's syndrome
Associated malignancy	Squamous cell cancers of lung, esophagus, head and neck. Breast cancer; more rarely ovarian cancer	Small cell lung cancer and squamous cell cancer of head and neck	Small cell lung cancer, bronchial carcinoid, medullary thyroid cancer, pancreatic islet cell tumors, pheochromocytoma
Presentation	Muscle weakness, cardiac arrhythmias, nausea and vomiting, renal failure	Hyponatremia, ↓ serum osmolarity, inappropriate ↑ urine osmolarity, euvoolemia, and normal thyroid and adrenal function	Hypokalemia, alkalosis, hypertension, psychosis
Etiology	↑ Release of parathyroid hormone-related peptides and other cytokines	Production of arginine vasopressin by tumor	Abnormally high secretion of ACTH or CRH
Management	Treat malignancy, hydrate, diuresis, calcitonin, steroids, bisphosphonates	Treat malignancy, fluid restriction, demeclocycline	Dexamethasone suppression (for some tumors), bromocriptine, ketoconazole

ACTH adrenocorticotrophic hormone; CRH corticotrophin-releasing hormone

Based on data from ref. [86]

encountered. The remainder of this chapter will be devoted to the discussion of the carcinoid syndrome (a paraendocrine syndrome) and LES (a paraneoplastic syndrome). Although not common, both have important implications for the anesthesiologist.

Carcinoid Tumors

Carcinoid tumors are most commonly found in the gastrointestinal tract where they often present due to bowel obstruction or are discovered due to symptoms of carcinoid syndrome. Primary carcinoids outside of the GI tract have originated in the ovary [87], liver [88, 89], and thymus [90, 91], but the most common extra-intestinal location is the lung [92].

Bronchial carcinoids account for 2–5% of primary lung tumors, however, this makes up 20–30% of all carcinoids [92]. Seventy-five percent of bronchial carcinoids are centrally located therefore present with symptoms of post-obstructive pneumonia, hemoptysis, and dyspnea [93]. The remaining one-quarter occur peripherally in the lung, are asymptomatic, and are usually detected on routine chest radiography [93].

The most fascinating aspect of carcinoid tumors remains their secretory nature. It is estimated that 15–20% of all carcinoids give rise to paraendocrine syndromes, most notably the “carcinoid syndrome” [92]. Carcinoid tumors may secrete well over a dozen compounds, including serotonin, histamine, catecholamines (norepinephrine and dopamine), bradykinins, ACTH, GHRH, and others [94]. The secretory behavior of the tumor as well as the exposure to the systemic circulation determines whether a paraendocrine syndrome will develop. Enzymes capable of metabolizing the secretory products are present in the liver and lung. Tumor products secreted from gastrointestinal carcinoids travel to the liver via the portal circulation and are inactivated before a paraendocrine syndrome can be manifested. If metastases to the liver occur, secretory products may enter the systemic circulation via the hepatic vein and exert their systemic effects.

The carcinoid syndrome is classically described as the triad of flushing, diarrhea, and bronchospasm. In addition, patients complain of sweating, tachycardia, and dyspnea. Diarrhea can be particularly troublesome, occurring up to 30 times per day and causing fluid and electrolyte disturbances as well as weight loss [95]. The limerick below aptly describes the classic patient with carcinoid syndrome.

This man was addicted to moanin',
Confusion, edema and groanin',
Intestinal rushes,
Great tricolored blushes,
And died from too much serotonin

Samuel A. Wells [96]

Carcinoid crises are life-threatening, severe episodes of profound flushing, hypertension or hypotension, arrhythmia, bronchoconstriction, and alteration of mental status [95, 97]. Crisis may be triggered by emotional stress, heat, cold, ingestion of certain foods (alcohol, chocolate), straining, as well as physical manipulation of the tumor (abdominal palpation or biopsy) [94, 98].

A significant proportion of carcinoid tumors occur in the bronchus and, less commonly, in the thymus [91] and therefore will be encountered by the thoracic anesthesiologist. In contrast to gastrointestinal carcinoids, bronchial and thymic carcinoids are seldom secretory. Less than 5% of bronchial carcinoids exhibit paraendocrine syndromes [93]. When the rare secretory bronchial carcinoid is encountered, the symptoms described above may be unusually severe and prolonged. In addition to the classical carcinoid syndrome, bronchial and thymic carcinoids may secrete exclusively ACTH (causing Cushing's syndrome) or even GHRH (causing acromegaly) [99–103]. In fact, bronchial and thymic carcinoids are the most common causes of ectopic ACTH outside of the pituitary and adrenal glands [90]. Therefore, although the lung is the most common location of extra-intestinal carcinoids, secretion of metabolically active compounds is rare. Although often non-secretory, the vascularity of these tumors should be kept in mind in the cases of bronchoscopy and particularly

biopsy. Severe hemorrhage can result and may require emergent thoracotomy [104].

Advanced carcinoid disease is associated with fibrosis which is attributed to the mitogenic effect of serotonin on smooth muscle and connective tissue. In the abdomen, this may present as retroperitoneal or omental fibrosis, but in the cardiopulmonary system, this can lead to pulmonary hypertension and carcinoid heart disease [94, 105].

Carcinoid heart disease manifests as right-sided valvulopathy, most notably severe tricuspid regurgitation with progressive volume overload of the right-sided heart chambers. Its onset is usually preceded by a history of carcinoid syndrome indicating passage of secretory products into the systemic circulation and therefore into the chambers of the right heart [106]. Although most often attributed to serotonin, the reduction of serotonin levels by medical management does not alter progression of heart disease indicating that other secretory products are involved in the pathophysiology [107]. The left-sided cardiac chambers are considered to be “protected” by the pulmonary circulation which metabolizes the carcinoid products; however, in the presence of a secretory bronchial carcinoid or a right to left shunt, left-sided carcinoid heart disease is seen and manifests as regurgitant mitral and aortic valve lesions [107]. With time, the right ventricle becomes hypokinetic and right-sided heart failure develops with severe dyspnea, ascites, and peripheral edema. Management options are limited. Medical therapies used for left-sided heart failure often have limited effect or may even worsen right-sided heart failure [106, 107]. Surgical management is the only option and carries a 35% mortality rate [104].

Medical management of carcinoid syndrome has been revolutionized by the discovery that the tumor cells often possess somatostatin receptors. Somatostatin, or its longer-acting analog octreotide, are able to suppress tumor secretion and alleviate the symptoms of carcinoid syndrome in most patients [108]. Prior to the introduction of octreotide, management of the carcinoid syndrome involved a variety of anti-histamine and anti-serotonergic drugs with limited efficacy. Despite the ability to control symptoms of carcinoid disease, octreotide has no effect on tumor growth. Use of chemotherapeutic agents has had limited success in carcinoid tumors making surgical resection the definitive therapy.

Preoperative assessment of patients with carcinoid tumors is influenced by whether the tumor is secretory or not. This can be determined by history or by urinary levels of 5-HIAA (serotonin metabolite) in the case of asymptomatic patients. A nonsecretory tumor has less significance for the anesthesiologist. In the case of carcinoid syndrome, the history should ascertain the severity of symptoms as well as how well they are controlled with medical therapy. The severity of symptoms does not predict the intraoperative course; however, it is helpful to know that the tumor is responsive to octreotide [109]. Physical examination should look for signs of right-sided valvulopathy and heart failure. Preop-

erative investigations should include complete blood count, electrolytes, liver function tests, and creatinine as well as measurement of blood glucose. All patients should have an electrocardiogram and chest X-ray to screen for cardiac disease; however, an echocardiogram is the definitive test for carcinoid heart disease.

Perioperative care of the patient with carcinoid syndrome involves avoidance of triggers and preparation to manage crisis, particularly at times of tumor manipulation.

Preoperative optimization should correct hypovolemia and electrolyte imbalances. Preoperative sedation with a benzodiazepine (lorazepam sublingual 2 mg, 90 min preoperatively) is highly recommended and consideration may be given to use of cyproheptadine (4 mg; antihistamine and anti-serotonergic) as well. Patients should receive octreotide 50–100 µg sc BID for at least 24 h prior to induction with an additional 100 µg sc 1 h preoperatively [104, 107, 109].

Intraoperatively, monitors should be placed while the patient is awake. In addition to standard monitors, invasive blood pressure monitoring is required and central access is indicated for CVP monitoring, rapid administration of drugs, fluids, and blood if required. Temperature monitoring and body warmers should be used as hypothermia is a trigger of crises. In the presence of cardiac disease, transesophageal echocardiography should be readily available. Octreotide infusion at 100–250 µg/h is recommended [97, 104] and may be started once in the operating room. A smooth induction and blunting of airway reflexes for intubation is ideal. Etomidate and sodium thiopental may not blunt airway reflexes as well as propofol and histamine release by sodium thiopental may trigger crisis and is best avoided. Nonhistamine releasing opioids such as fentanyl or remifentanil may be used with good results [110]. The use of NDMR is safe provided that histamine release is avoided. Succinylcholine use is controversial. Some practitioners strictly avoid it due to concern over histamine release and concern over precipitating a crisis secondary to fasciculations [97, 104]. In a review of 21 patients with carcinoid syndrome, Veall et al. [111] used succinylcholine in half of the patients uneventfully. Therefore, in optimized patients, the use of succinylcholine should not be considered contraindicated when airway or other concerns make it the best choice of muscle relaxant.

Intraoperatively, electrolytes and glucose should be monitored and hyperglycemia may require insulin infusion. Octreotide, diluted to 10–50 µg/mL should be readily available for emergency use in doses of 50–100 µg and titrated to response.

Carcinoid crisis may manifest as profound hypertension or hypotension accompanied by bronchospasm. Hypertension may be treated by increasing anesthetic depth, administering a bolus of short-acting opioid [111], use of β-blockade (metoprolol or esmolol) [109], or administration of octreotide. Kataserin, a selective serotonin antagonist with α-1 blocking effects has also been described as useful (dose 5–10 mg) but has Vaughn-Williams class I and III antiarrhythmic effects

and may prolong the QT-interval [106, 109]. Cyproheptadine (1 mg) or methotrimeprazine (2.5 mg) are serotonin antagonists which have also been described for the management of hypertensive carcinoid crisis.

Profound hypotension is a more common manifestation of crisis intraoperatively and may be severe. The treatment of choice is octreotide boluses as described above. Intravenous octreotide reaches peak effect after 4 min; there are no significant side effects and doses may need to be escalated until a response is seen [111]. Vasopressin or phenylephrine have also been described as an additional therapy if hypotension is refractory [109, 112]. Additional management of hypotension includes fluid resuscitation, reduction of anesthetic depth, and cessation of surgical manipulation. Catecholamines are usually avoided in the treatment of hypotension as they may precipitate further crisis; however, recent data suggest they may be used in patients who have been optimized with somatostatin analogs [107]. If necessary, small boluses should be administered and the response observed carefully. In addition to the above, calcium, angiotensin, and milrinone are also considered safe [97, 111].

The management of bronchospasm with salbutamol is another area of controversy. Noncatecholamine bronchodilators (ipratropium bromide), steroids, antihistamines, and octreotide have been suggested as effective for crisis-associated bronchospasm [109]. Others describe the safe and effective use of salbutamol and advocate its use despite sympathomimetic activity [87, 111]. While noncatecholamine bronchodilators should be considered first, salbutamol is not contraindicated particularly in an optimized patient with bronchospasm.

Neuraxial anesthesia is controversial in a patient population at risk for acute hemodynamic instability, however, both epidural [110, 113] and spinal anesthesia [114] have been described even in the presence of severe carcinoid heart disease. Keys to this approach noted by all authors included preoperative optimization with octreotide, adequate volume loading, and the minimization of hemodynamic changes by careful drug selection.

Postoperatively, delayed awakening has been described and attributed to the high serotonin levels. Patients require an intensive care environment where hemodynamic monitoring and continuation of drug infusions are possible. Manifestations of carcinoid syndrome may continue due to residual tumor or unresected metastases. Octreotide infusions should be continued and weaned slowly while monitoring for manifestations of residual secretory activity. Postoperative analgesia is imperative to avoid triggering crisis and for this reason, the benefits of a carefully titrated epidural infusion may outweigh the risks.

Lambert–Eaton Myasthenic Syndrome (LEMS)

LEMS is the most common of the classical paraneoplastic syndromes [115]. Fifty to sixty percent of patients presenting with LEMS will subsequently be diagnosed with a malignancy,

TABLE 15.11. Myasthenia gravis vs. Lambert–Eaton syndrome.

Feature	Myasthenia gravis	Eaton–Lambert syndrome
Most commonly associated malignancy	Thymoma (40%)	Small cell lung cancer (1–3%)
Antibody target	Acetylcholine receptor	Voltage-gated calcium channel
Area of NMJ affected	Postsynaptic membrane	Presynaptic membrane
Common presenting feature	Ocular and bulbar weakness	Limb weakness, oculomotor sparing
Ocular and bulbar muscle involvement	Common	Rare
Autonomic dysfunction	None	Common
Deep tendon reflexes	Normal	Reduced
Strength improved by	Rest, sleep	Exercise

most commonly small cell lung cancer (SCLC), within 2 years [116]. Three percent of patients with SCLC will experience LEMS [117].

LES bears a striking resemblance to MG at first glance, but there are many important differences (Table 15.11). While MG is a disease affecting the postsynaptic membrane, LES is due to a reduction in acetylcholine release from the presynaptic nerve terminal [118–120]. An autoimmune attack directed against the voltage-gated calcium channels of the presynaptic nerve terminal reduces calcium entry into the presynaptic nerve terminal. As a result of reduced calcium influx, there is markedly reduced acetylcholine release leading to symptoms of LEMS.

The most common presenting symptoms of LEMS are proximal lower extremity weakness. Many also experience autonomic symptoms such as dry mouth, impotence, constipation, and orthostatic hypotension. Ocular and bulbar muscle involvement may be present but is often mild and usually not the presenting feature. Respiratory muscle weakness can occur but usually as a late complication [116].

Management of LEMS is usually medical as patients with SCLC are often not operative candidates for resection of their malignancy. 3,4-diaminopyridine is a potassium-channel blocking drug which causes the depolarization of the presynaptic nerve terminal to be prolonged. This allows time for increased calcium influx which results in increased acetylcholine release and greater clinical strength [121]. There may also be a role for IVIG and plasmapheresis in some cases [87].

Patients with LEMS presenting for anesthesia are very sensitive to both succinylcholine and NDMR [121]. Therapy with 3,4-diaminopyridine should be continued up to the time of surgery. The use of paralytics should be minimized and, if necessary, should be titrated in very small doses and monitored closely. Reversal of neuromuscular blockade by usual means is seldom effective. The administration of 3,4-diaminopyridine concomitantly with reversal agents has been met with some success [122, 123]. Additional consideration should be given to the potential for autonomic disturbances and provision should be made preoperatively for postoperative ventilation if required.

Clinical Case Discussion

Case: A 32-year old female presents for preoperative assessment. She is booked for a transcervical thymectomy for MG. In addition to the usual preoperative assessment, consider:

- What additional information, specific to this patient, should be gathered at the preoperative anesthesia consultation
- Appropriate investigations
- How you will optimize her for the upcoming surgery
- What premedication she will require including dosing of her current medications
- Appropriate postoperative disposition
- Your anesthetic technique of choice including acute postoperative pain management

What Additional Information, Specific to this Patient, Should be Gathered at the Preoperative Anesthesia Consultation?

In addition to the usual elements of a preoperative consultation, the preoperative visit should serve to characterize the severity of MG in this patient as well as determine if there are any mediastinal compressive symptoms. A history of associated autoimmune disorders should also be sought.

Determine when the patient was diagnosed with MG and how the disease has progressed. Determine if the symptoms have been purely ocular or if they have involved bulbar muscles (putting the patient at risk for dysphagia and aspiration), axial or limb muscles, or if the patient has had any episodes of respiratory failure requiring ventilator support. Determine the management history, particularly the dose and frequency of pyridostigmine and what the consequences are of delaying a dose. Is there a history of steroid requirements or the use of any other immunosuppressants?

A history of palpitations, chest pain, or dyspnea on exertion as well as findings consistent with heart failure should be sought due to the possibility of cardiac involvement. The association with thyroid dysfunction, rheumatoid arthritis, and lupus should also prompt screening questions which may or may not require additional medical consultation and optimization.

To screen for a thymoma with mass effect, a history of orthopnea, supine dyspnea, or cough should be sought. Changes in voice (dysphonia, hoarseness), palpitations, syncope, edema of the face or tongue, and dysphagia are other signs of mediastinal compression; however, dysphagia and dysphonia may also be due to MG.

This patient has been diagnosed with MG for 5 years. She initially presented with oculobulbar symptoms which were well controlled with mestinon. Over the last few years, increasing doses of mestinon have been required eventually prompting the referral for surgical treatment. She does not have any associated autoimmune disorders and denies all symptoms of mass compression. To her knowledge, there is no thymoma present. She

takes 80 mg of pyridostigmine every 4 h and feels weakness if she is more than an hour late with her dose. Her usual first dose is taken at around 6 o'clock in the morning.

Appropriate Investigations

Bloodwork: CBC (pernicious anemia) and blood cross-match are mandatory. Strongly consider electrolytes and creatinine, coagulation profile, and TSH as well.

Imaging must be reviewed, CXR and chest CT for the presence of any thymoma.

Blood work in this patient is all within normal limits. Her TSH is normal. The radiologist's reports do not mention any sign of aspiration pneumonia nor any thymoma causing compression of cardiopulmonary structures.

How You Will Optimize Her for the Upcoming Surgery

Confirm that the patient's neurologist is aware of the upcoming surgery and discuss possible plasmaphoresis or IVIG to optimize the patient's muscular strength and minimize the chances of perioperative respiratory failure and need for postoperative ventilation. Pyridostigmine should be continued up to the day of surgery and the surgery should be scheduled first thing in the morning. The patient should be instructed to take their morning dose of pyridostigmine as close to the time of surgery as is possible. If the surgery takes longer than expected, an intravenous supplemental acicholinesterase may be given or an additional dose of oral pyridostigmine may be given via a nasogastric tube. No premedication with sedating effects should be ordered.

The Anesthetic Technique of Choice Including Acute Postoperative Pain Management

General anesthesia with endotracheal intubation is the technique of choice under these circumstances. Induction with propofol and remifentanil is recommended (no neuromuscular blockade). Maintenance may be achieved with a volatile, such as Desflurane, or with a propofol infusion. Remifentanil may be used as an analgesic infusion. Pre- or intra-operative acetaminophen and nonsteroidal anti-inflammatory (such as naprosyn or ketorolac) should also be used and continued postoperatively. The surgeon should be asked to infiltrate the wound with local anesthesia at closure.

Appropriate Postoperative Disposition

Patients undergoing transcervical thymectomy for nonthymomatous MG have significantly less pain and respiratory dysfunction than patients undergoing transsternal thymectomy. Provided that the patient can be optimized preoperatively with plasmaphoresis or equivalent, an overnight stay in a regular ward is appropriate. Pain is likely to be manageable

with oral opioids and multimodal analgesia with acetaminophen and anti-inflammatories will be beneficial. Based on the history, optimization, and low analgesic requirements, the risk of postoperative respiratory failure is low. Pyridostigmine dosing must be continued and ongoing collaboration with neurology and the postoperative care team is important.

References

1. Souza CA, Muller NL. Imaging of the mediastinum. In: Patterson GA, Cooper JD, Deslauriers J, Lerut AEMR, Luketich JD, Rice TW, editors. Pearson's thoracic and esophageal surgery. 3rd ed. Philadelphia: Churchill Livingstone; 2008. p. 1477–505.
2. Souadjian JV, Enriquez P, Silverstein MN, et al. The spectrum of diseases associated with thymoma. *Arch Intern Med.* 1974;134:374–9.
3. Maggi G, Casadio C, Cavallo A, et al. Thymoma: results of 241 operated cases. *Ann Thorac Surg.* 1991;51:152–6.
4. Blumberg D, Burt ME, Bains MS, et al. Thymic carcinoma: current staging does not predict prognosis. *J Thorac Cardiovasc Surg.* 1998;115:303–9.
5. Miller BS, Rusinko RY, Fowler L. Synchronous thymoma and thymic carcinoid in a woman with multiple endocrine neoplasia type 1: case report and review. *Endocr Pract.* 2008;14:713–6.
6. Falkson CB, Bezjak A, Darling G, et al. The management of thymoma: a systematic review and practice guideline. *J Thorac Oncol.* 2009;4:911–9.
7. Tomaszek S, Wigle DA, Keshavjee S, et al. Thymomas: review of current clinical practice. *Ann Thorac Surg.* 2009;87:1973–80.
8. Lerro A, De Luca G. Giant thymolipoma causing cardiocompressive syndrome and chronic heart failure. *Ann Thorac Surg.* 2009;87:644.
9. Jiang X, Fang Y, Wang G. Giant thymolipoma involving both chest cavities. *Ann Thorac Surg.* 2009;87:1960.
10. Ceran S, Tulek B, Sunam G, et al. Respiratory failure caused by giant thymolipoma. *Ann Thorac Surg.* 2008;86:661–3.
11. Johnson SB, Eng TY, Graccone G, et al. Thymoma: update for the new millennium. *Oncologist.* 2001;6:239–46.
12. Korst RJ, Kansler AL, Christos PJ, et al. Adjuvant radiotherapy for thymic epithelial tumors: a systematic review and meta-analysis. *Ann Thorac Surg.* 2009;87:1641–7.
13. Girard N, Mornex F, Van Houtte P, et al. Thymoma. A focus on current therapeutic management. *J Thorac Oncol.* 2009;4:119–26.
14. Venuta F, Rendina EA, Coloni GF. Multimodality treatment of thymic tumors. *Thorac Surg Clin.* 2009;19:71–81.
15. Pascuzzi R. The history of myasthenia gravis. *Neurol Clin.* 1994;12:231–42.
16. Jolly F. Über myasthenia gravis pseudoparalytica. *Berliner Klin Wochenschr.* 1895;32:1.
17. Grob D, Brunner N, Namba T, et al. Lifetime course of myasthenia gravis. *Muscle Nerve.* 2008;37:141–9.
18. Engel AG, Lambert EH, Howard FM. Immune complexes (IgG and C3) at the motor end plate in myasthenia gravis: ultrastructural and light microscopic localization and electrophysiological correlations. *Mayo Clin Proc.* 1977;52:267–80.
19. Pestronk A, Drachman DB, Self SG. Measurement of junctional acetylcholine receptors in myasthenia gravis: clinical correlates. *Muscle Nerve.* 1985;8:245–51.
20. Drachman DB. Myasthenia gravis. *N Eng J Med.* 1994;330:1797–810.
21. Engel AG, Tsujihata M, Lindstrom JM, et al. The motor end plate in myasthenia gravis and in experimental autoimmune myasthenia gravis: a quantitative ultrastructural study. *Ann N Y Acad Sci.* 1976;274:60–79.
22. Thomas CR, Wright CD, Loehrer PG. Thymoma: state of the art. *J Clin Oncol.* 1999;17:2280–9.
23. Castleman B. The pathology of the thymus gland in myasthenia gravis. *Ann N Y Acad Sci.* 1966;135:496–505.
24. Osberman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. *Mt Sinai J Med.* 1971;38(6):497–537.
25. Gibson TC. The heart in myasthenia gravis. *Am Heart J.* 1975;90:389–96.
26. Johannessen KA, Mygland A, Gilhus NE, et al. Left ventricular function in myasthenia gravis. *Am J Cardiol.* 1992;69:129–32.
27. Hofstad H, Ohm O-J, Mork SJ, et al. Heart disease in myasthenia gravis. *Acta Neurol Scand.* 1984;70:176–84.
28. Daroff RB. The office tensilon test for ocular myasthenia gravis. *Arch Neurol.* 1986;43:842–4.
29. Osberman KE. Myasthenia gravis. New York: Grune & Stratton; 1958.
30. Jaretzki III A, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. *Ann Thorac Surg.* 2000;70:327–34.
31. Nicolle MW. Myasthenia gravis. *Neurologist.* 2002;8:2.
32. Baraka A. Anaesthesia and myasthenia gravis. *Can J Anaesth.* 1992;39(5):476–86.
33. Sathasivam S. Steroids and immunosuppressant drugs in myasthenia gravis. *Neurology.* 2008;4:317–27.
34. Pinching AJ, Peters DK. Remission of myasthenia gravis following plasma-exchange. *Lancet.* 1976;2:1373–6.
35. Gajdos P, Chevret S, Toyka KV. Intravenous immunoglobulin for myasthenia gravis. *Cochrane Database Syst Rev.* 2008, Issue 1. Art No.:CD002277. DOI: [10.1002/14651858.CD002277.pub3](https://doi.org/10.1002/14651858.CD002277.pub3).
36. Arsura E. Experience with intravenous immunoglobulin in myasthenia gravis. *Clin Immunol Immunopathol.* 1989;53:S170–9.
37. Blalock A, Mason MF, Morgan HJ, et al. Myasthenia gravis and tumors of the thymic region: report of a case in which the tumor was removed. *Ann Surg.* 1939;110:544–61.
38. Blalock A, Harvey AM, Ford FR, et al. The treatment of myasthenia gravis by removal of the thymus gland. *JAMA.* 1941;117:1529–33.
39. Blalock A. Thymectomy in the treatment of myasthenia gravis. Report of twenty cases. *J Thorac Surg.* 1944;13:316–39.
40. Mulder D, Graves M, Herrmann C. Thymectomy for myasthenia gravis: recent observations and comparisons with past experience. *Ann Thorac Surg.* 1989;48:551.
41. De Perrot M, Bril V, McRae K, et al. Impact of minimally invasive trans-cervical thymectomy on outcome of patients with myasthenia gravis. *Eur J Cardiothorac Surg.* 2003;24:677–83.
42. Bachmann K, Burkhardt D, Schreiter I, et al. Long term outcome and quality of life after open and thoracoscopic thymectomy for myasthenia gravis: analysis of 131 patients. *Surg Endosc.* 2008;22:2470–7.
43. Prokakis C, Koletsis E, Salakou S, et al. Modified maximal thymectomy for myasthenia gravis: effect of maximal resection on late neurologic outcome and predictors of disease remission. *Ann Thorac Surg.* 2009;88:1638–45.

44. Pompeo E, Tacconi F, Massa R, et al. Long-term outcome of thoracoscopic extended thymectomy for nonthymomatous myasthenia gravis. *Eur J Cardiothorac Surg.* 2009;36:164–9.
45. Gronseth GS, Barohn RJ. Practice parameter: thymectomy for autoimmune myasthenia gravis (an evidence-based review): report of the quality standards subcommittee of the American Academy of Neurology. *Neurology.* 2000;55:7–15.
46. Singhal S, Kaiser LR. Surgery for myasthenia gravis. In: Patterson GA, Cooper JD, Deslauriers J, Lerut AEMR, Luketich JD, Rice TW, editors. *Pearson's thoracic and esophageal surgery.* 3rd ed. Philadelphia: Churchill Livingstone; 2008. p. 1549–61.
47. Howard JF. Physician issues. In: Howard JF, editor. *Myasthenia gravis. A manual for the health care provider.* St. Paul: Myasthenia Gravis Foundation of America; 2008. p. 8–30.
48. Gracey DR, Divertie MB, Howard FM. Mechanical ventilation for respiratory failure in myasthenia gravis. *Mayo Clin Proc.* 1983;58:597602.
49. Leventhal SR, Orkin FK, Hirsh RA. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology.* 1980;53:26–30.
50. Grant RP, Jenkins LC. Prediction of the need for postoperative mechanical ventilation of myasthenia gravis: thymectomy compared to other surgical procedures. *Can Anaesth Soc J.* 1982;29(2):112–6.
51. Eisenkraft JB, Papatestas AE, Kahn CH, et al. Predicting the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology.* 1986;65:79–82.
52. Gracey DR, Divertie MB, Howard FM, et al. Postoperative respiratory care after transsternal thymectomy in myasthenia gravis. *Chest.* 1984;86(1):67.
53. Eisenkraft JB, Papatestas AE, Pozner JN, et al. Predictors of respiratory failure following transcervical thymectomy. *Ann N Y Acad Sci.* 1987;505:888–90.
54. Younger DS, Braun NMT, Jaretzki III A, et al. Myasthenia gravis: determinants for independent ventilation after transsternal thymectomy. *Neurology.* 1984;34:336–40.
55. El-Bawab H, Hajjar W, Rafay M, et al. Plasmapheresis before thymectomy in myasthenia gravis: routine versus selective protocols. *Eur J Cardiothorac Surg.* 2009;35:392–7.
56. Spence PA, Morin JE, Katz M. Role of plasmapheresis in preparing myasthenic patients for thymectomy: initial results. *Can J Surg.* 1984;27:303–5.
57. Baraka A, Taha S, Yazbeck V, et al. Vecuronium block in the myasthenic patient. Influence of anticholinesterase therapy. *Anesthesia.* 1993;48:588–90.
58. Ropper AH, Samuels MA. Myasthenia gravis and related disorders of the neuromuscular junction. In: Adams and Victor's principles of neurology. 9th ed. New York: McGraw-Hill; 2009. p. 1405–1421.
59. Girnar DS, Weinreich AI. Anesthesia for transcervical thymectomy in myasthenia gravis. *Anesth Analg.* 1976;55:13–7.
60. Krucylak PE, Naunheim KS. Preoperative preparation and anesthetic management of patients with myasthenia gravis. *Semin Thorac Cardiovasc Surg.* 1999;11(1):47–53.
61. Kim JM, Mangold J. Sensitivity to both vecuronium and neostigmine in a seronegative myasthenic patient. *Br J Anaesth.* 1989;63:497–500.
62. Lumb AB, Calder I. Cured myasthenia gravis and neuromuscular blockade. *Anesthesia.* 1989;44:828–30.
63. Azar I. The response of patients with neuromuscular disorders to muscle relaxants: a review. *Anesthesiology.* 1984;61:173–87.
64. Abel M, Eisenkraft JB. Anesthetic implications of myasthenia gravis. *Mt Sinai J Med.* 2002;69(1–2):31–7.
65. Blitt CD, Wright WA, Peat J. Pancuronium and the patient with myasthenia gravis. *Anesthesiology.* 1975;42:624–6.
66. Book WJ, Abel M, Eisenkraft JB. Anesthesia and neuromuscular diseases. *Anesth Clin North Am.* 1996;14:515–42.
67. Eisenkraft JB, Book JW, Mann SM, et al. Resistance to succinylcholine in myasthenia gravis: a dose-response study. *Anesthesiology.* 1988;69:760–3.
68. Wainwright AP, Brodrick PM. Suxamethonium in myasthenia gravis. *Anesthesia.* 1987;42:950–7.
69. Baraka A, Baroody M, Yazbeck V. Repeated doses of suxamethonium in the myasthenic patient. *Anesthesia.* 1993;48:782–4.
70. Nilsson E, Muller K. Neuromuscular effects of isoflurane in patients with myasthenia gravis. *Acta Anaesthesiol Scand.* 1990;34:126–31.
71. Kiran U, Choudhury M, Saxena N, et al. Sevoflurane as a sole anesthetic agent for thymectomy in myasthenia gravis. *Acta Anaesthesiol Scand.* 2000;44:351–3.
72. Nishi M, Nakagawa H, Komatsu R, et al. Neuromuscular effects of sevoflurane in a patient with myasthenia gravis. *J Anaesth.* 1993;7:325–8.
73. Madi-Jebara S, Yazigi A, Hayek G, et al. Sevoflurane anesthesia and intrathecal sufentanil-morphine for thymectomy in myasthenia gravis. *J Clin Anesth.* 2002;14:558–9.
74. Gritt P, Carrara B, Khotcholava M, et al. The use of desflurane or propofol in combination with remifentanil in myasthenic patients undergoing a video-assisted thoracoscopic-extended thymectomy. *Acta Anaesthesiol Scand.* 2009;53:380–9.
75. Hubler M, Litz RJ, Albrecht DM. Combination of balanced and regional anesthesia for minimally invasive surgery in a patient with myasthenia gravis. *Eur J Anaesth.* 2000;17:325–8.
76. Sener M, Bilen A, Bozdogan N, et al. Laryngeal mask airway insertion with total intravenous anesthesia for transsternal thymectomy in patients with myasthenia gravis: a report of five cases. *J Clin Anesth.* 2008;20:206–9.
77. Mekis D, Kamenik M. Remifentanil and high thoracic epidural anaesthesia: a successful combination for patients with myasthenia gravis undergoing transsternal thymectomy. *Eur J Anaesth.* 2005;22:397–9.
78. Bouaggad A, Bouderka MA, Abaassi O. Total intravenous anesthesia with propofol for myasthenic patients. *Eur J Anaesth.* 2005;22:392–402.
79. De Jose Maria B, Carrero E, Sala X. Myasthenia gravis and regional anesthesia. *Can J Anaesth.* 1995;42(2):178.
80. Matsuo S, Rao DB, Chaudry I, et al. Interaction of muscle relaxants and local anesthetics at the neuromuscular junction. *Anesth Analg.* 1978;57:580–7.
81. Burgess FW, Wilcosky B. Thoracic epidural anesthesia for transsternal thymectomy in myasthenia gravis. *Anesth Analg.* 1989;69:529–31.
82. Chevally C, Spiliopoulos A, de Perrot M, et al. Perioperative medical management and outcome following thymectomy for myasthenia gravis. *Can J Anesth.* 2001;48:446–51.
83. Akapolat N, Tilgen H, Gursoy F, et al. Thoracic epidural anesthesia and analgesia with bupivacaine for transsternal thymectomy for myasthenia gravis. *Eur J Anesthesiol.* 1997;14:220–3.

84. Kirsch JR, Diringer MN, Borel CO, et al. Preoperative lumbar epidural morphine improves postoperative analgesia and ventilator function after transternal thymectomy in patients with myasthenia gravis. *Crit Care Med.* 1991;12:1474–9.
85. Nilsson E, Perttunen K, Kalso E. Intrathecal morphine for poststernotomy pain in patients with myasthenia gravis: effect on respiratory function. *Acta Anaesthesiol Scand.* 1997;41:549–56.
86. Pierce ST. Paraendocrine syndromes. *Curr Opin Oncol.* 1993;5:639–45.
87. Toothaker TB, Rubin M. Paraneoplastic neurological syndromes. *Neurologist.* 2009;15:21–33.
88. Tohyama T, Matsui K, Kitagawa K. Primary hepatic carcinoid tumor with carcinoid syndrome and carcinoid heart disease: a case report of a patient on long-term follow-up. *Intern Med.* 2005;44:958–62.
89. Zhang A, Xiang J, Zhang M, et al. Primary hepatic carcinoid tumors: clinical features with an emphasis on carcinoid syndrome and recurrence. *J Int Med Res.* 2008;36:848–59.
90. Claret C, Chillaron JJ, Flores JA, et al. Carcinoid tumor of the thymus associated with Cushing's syndrome and dysgeusia: case report and review of the literature. *Endocrine.* 2010;37:1–5.
91. De Perrot M, Spiliopoulos A, Fischer S, et al. Neuroendocrine carcinoma (carcinoid) of the thymus associated with Cushing's syndrome. *Ann Thorac Surg.* 2002;73:675–81.
92. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. *Cancer.* 2003;97:934–59.
93. Gustafsson BI, Kidd M, Chan A. Bronchopulmonary neuroendocrine tumors. *Cancer.* 2008;113:5–21.
94. Lips CJM, Lentjes EGWM, Hoppenre JWM. The spectrum of carcinoid tumors and carcinoid syndromes. *Ann Clin Biochem.* 2003;40:612–27.
95. Ghevariya V, Malieckal A, Ghevariya N, et al. Carcinoid tumors of the gastrointestinal tract. *South Med J.* 2009;102:1032–40.
96. Wells SA. Current problems in surgery. Forward. *Curr Probl Surg.* 2006;43:382.
97. Dierdorf SF. Carcinoid tumor and carcinoid syndrome. *Curr Opin Anaesthesiol.* 2003;16:343–7.
98. Bendelow J, Apps E, Jones LE, et al. Carcinoid syndrome. *Eur J Surg Oncol.* 2008;34:289–96.
99. Athanassiadi K, Exarchos D, Tsagarakis S, et al. Acromegaly caused by ectopic growth-hormone-releasing hormone secretion by a carcinoid bronchial tumor: a rare entity. *J Thorac Cardiovasc Surg.* 2004;128:631–2.
100. Scheithauer BW, Carpenter PC, Block B, et al. Ectopic secretion of a growth hormone-releasing factor. Report of a case of acromegaly with bronchial carcinoid tumor. *Am J Med.* 1984;76:605–16.
101. Shrager JB, Wright CD, Wain JC, et al. Bronchopulmonary carcinoid tumors associated with Cushing's syndrome: a more aggressive variant of typical carcinoid. *J Thorac Cardiovasc Surg.* 1997;114:367–75.
102. Malchoff CD, Orth DN, Abboud C, et al. Ectopic ACTH syndrome caused by a bronchial carcinoid tumor responsive to dexamethasone, metyrapone, and corticotrophin-releasing factor. *Am J Med.* 1988;84(4):760–4.
103. Scanagatta P, Montresor E, Pergher S, et al. Cushing's syndrome induced by bronchopulmonary carcinoid tumors: a review of 98 cases and our experience of two cases. *Chir Ital.* 2004;56(1):63–70.
104. Fischer S, Kruger M, McRae K, et al. Giant bronchial carcinoid tumors: a multidisciplinary approach. *Ann Thorac Surg.* 2001;71:386–93.
105. Modlin IM, Shapiro MD, Kidd M. Carcinoid tumors and fibrosis: an association with no explanation. *Am J Gastroenterol.* 2004;99:2466–78.
106. Anderson AS, Krauss D, Lang R. Cardiovascular complications of malignant carcinoid disease. *Am Heart J.* 1997;134:693–702.
107. Bernheim AM, Connolly HM, Hobday TJ, et al. Carcinoid heart disease. *Prog Cardiovasc Dis.* 2007;49:439–51.
108. Kvols LK, Moertel CG, O'Connell MJ, et al. Treatment of malignant carcinoid syndrome. Evaluation of a long-acting somatostatin analogue. *N Engl J Med.* 1986;315(11):663–6.
109. Vaughan DJA, Brunner MD. Anesthesia for patients with carcinoid syndrome. *Int Anesthesiol Clin.* 1997;35:129–42.
110. Farling PA, Durairaj AK. Remifentanil and anaesthesia for carcinoid syndrome. *Br J Anaesth.* 2004;92:893–5.
111. Veall GRQ, Peacock JE, Bax NDS, et al. Review of the anaesthetic management of twenty-one patients undergoing laparotomy for carcinoid syndrome. *Br J Anaesth.* 1994;72:335–41.
112. Cortinez LI. Refractory hypotension during carcinoid resection surgery. *Anesthesia.* 2000;55:505–6.
113. Monteith K, Roaseg OP. Epidural anaesthesia for transurethral resection of the prostate in a patient with carcinoid syndrome. *Can J Anaesth.* 1990;37:349–52.
114. Orbach-Zinger S, Lombroso R, Eidelman LA. Uneventful spinal anesthesia for a patient with carcinoid syndrome managed with long-acting octreotide. *Can J Anaesth.* 2002;49:678–81.
115. Darnell RB, Posner JB. Paraneoplastic syndromes affecting the nervous system. *Semin Oncol.* 2006;33:270–98.
116. O'Neill JH, Murray NM, Newsom-Davis J. The Lambert-Eaton myasthenic syndrome. A review of 50 cases. *Brain.* 1988;111:577–96.
117. Elrington GM, Murray NM, Spiro SG, et al. Neurological paraneoplastic syndromes in patients with small cell lung cancer. A prospective survey of 150 patients. *J Neurol Neurosurg Psychiatry.* 1991;54:764–77.
118. Lambert EH, Elmqvist D. Quantal components of end-plate potentials in the myasthenic syndrome. *Ann N Y Acad Sci.* 1971;15:183–99.
119. Elmqvist D, Lambert EH. Detailed analysis of neuromuscular transmission in a patient with the myasthenic syndrome sometimes associated with bronchogenic carcinoma. *Mayo Clin Proc.* 1968;43:689–713.
120. Molenaar PC, Newsom-Davis J, Polak RL, et al. Eaton-Lambert syndrome: acetylcholine and choline acetyltransferase in skeletal muscle. *Neurology.* 1982;32:1061–5.
121. O'Neill G. Acquired disorders of the neuromuscular junction. *Int Anesthesiol Clin.* 2006;44:107–21.
122. Telford RJ, Hollway TE. The myasthenic syndrome: anaesthesia in a patient. *Br J Anaesth.* 1990;64:363–6.
123. Small S, Ali HH, Lennon VA, et al. Anesthesia for an unsuspected Lambert-Eaton myasthenic syndrome with autoantibodies and occult small cell lung carcinoma. *Anesthesiology.* 1992;76:142–5.

16

Lung Isolation

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Key Points

- During the preoperative period, review of the posterior-anterior chest radiograph is necessary to measure the tracheal width and also appreciate the pattern of the tracheobronchial anatomy to determine what device and size to use.
- The left-sided DLT is the most common device used for lung isolation because of its greater margin of safety.
- The use of bronchial blockers is indicated in patients who present with difficult airways and require lung isolation.
- Patients with a tracheostomy in place requiring lung isolation are best managed with the use of an independent bronchial blocker and flexible fiberoptic bronchoscopy.
- Flexible fiberoptic bronchoscopy is the recommended method to achieve optimal position of lung isolation devices, first in supine position, later in lateral decubitus, or whenever a malposition occurs.

Introduction

Lung separation techniques are used to provide one-lung ventilation (OLV) in patients undergoing thoracic, mediastinal, cardiac, vascular, or esophageal procedures [1, 2]. Lung separation can be achieved with two different techniques. The first involves a device made of disposable polyvinylchloride material, the double-lumen endotracheal tube (DLT) [3]. The DLT is a bifurcated tube with both an endotracheal and an endobronchial lumen and can be used to achieve isolation of either the right or left lung. The second technique involves blockade of a mainstem bronchus to allow lung collapse distal to the occlusion [4]. Currently, there are different bronchial blockers available to facilitate lung separation collapse; these devices are either attached to a single-lumen endotracheal tube with an enclosed bronchial blocker (Torque Control Blocker Univent) (Vitaid, Lewiston, NY) [5] or are used independently over a standard single-lumen endotracheal tube, as with the

TABLE 16.1. Indications for lung isolation with a double-lumen endotracheal tube (DLT) or a bronchial blocker.

A. Indications for lung isolation with the use of a DLT				
<ul style="list-style-type: none"> • Protection of one lung from a contralateral contamination <ul style="list-style-type: none"> • Lung abscess • Lung cyst • Pulmonary hemorrhage • Bronchopulmonary lavage • Pulmonary alveolar proteinosis • Control and continuity of the airway gas exchange <ul style="list-style-type: none"> • Bronchopleural fistula • Bronchial disruption (i.e., laceration with a knife) • Pneumonectomy 				
B. Indication for lung isolation with the use of a DLT or a bronchial blocker				
<ul style="list-style-type: none"> • Any operation that requires surgical exposure through the chest cavity with lung collapse <ul style="list-style-type: none"> • Video-assisted thoracoscopic surgery • Lobectomy bilobectomy • Mediastinal mass resection through the chest (selective cases) • Esophageal surgery • Orthopedic procedures (spine surgery involving chest) • Minimally invasive cardiac surgery 				
C. Specific indications for bronchial blockers				
<ul style="list-style-type: none"> • Difficult airways • Limited mouth opening <ul style="list-style-type: none"> – Nasotracheal intubation • Awake orotracheal intubation • Already intubated patient requiring lung isolation • Tracheostomy patient requiring lung isolation • Selective lobar blockade • Potential for mechanical ventilation in the postoperative period 				

wire-guided endobronchial blocker (Arndt® blocker) [6] (Cook Critical Care, Bloomington, IN), the Cohen tip-deflecting endobronchial blocker [7] (Cook Critical Care, Bloomington, IN), or the Fuji Uni-blocker® [8] (Fuji Corp, Tokyo, Japan). There are a number of recognized indications for OLV. In practice, the most common indications for lung separation are (1) for surgical exposure, (2) for prevention of contamination to the contralateral lung from bleeding pus material or saline lavage (abscess, hemoptysis, bronchiectasis, and lung lavage), and (3) during differential lung ventilation or for continuity of the airway gas exchange such as with bronchopleural fistula. Table 16.1 describes common indications for lung isolation with a DLT or a bronchial blocker.

Double-Lumen Endotracheal Tubes

Currently, all DLTs are based on a design suggested by Carlens and Björk [9]. There are two versions of DLTs, left-sided and a right-sided, which are designed to accommodate the unique anatomy of each mainstem bronchus [10]. DLTs are available from different manufacturers: Mallinckrodt Broncho-Cath (St. Louis, MO) is the most common brand name in North America; there is also the Sheridan Sher-I-Bronch (Argyle, NY) and DLTs from Rüsch (Duluth, GA) and Portex (Keene, NH). The sizes of the DLTs vary among manufacturers; the

TABLE 16.2. Displays the external and internal diameters of the different sizes of DLTs and the size of the flexible fiberoptic bronchoscope recommended.

DLT French size (F)				
F size	OD (mm)	Bronchial ID (mm)	Trachea ID (mm)	FOB size OD (mm)
26	8.7	3.5	3.5	2.2
28	9.3	3.2	3.1	2.2
32	10.7	3.4	3.5	2.2
35	11.7	4.3	4.5	3.5 or 4.2
37	12.3	4.5	4.7	3.5 or 4.2
39	13.0	4.9	4.9	3.5 or 4.2
41	13.7	5.4	5.4	3.5 or 4.2

OD outer diameter; ID internal diameter; FOB fiberoptic bronchoscope

smallest available is 26 French (F) followed by 28, 32, 35, 37, 39, and 41 F. Table 16.2 displays the external and internal diameters of the different sizes of DLTs and the size of the flexible fiberoptic bronchoscope recommended (of note, the size of the DLTs varies among manufacturers). The ones described in this table are: Mallinckrodt Broncho-Cath, Sher-I-Bronch, and Rüsch.

Size Selection

Regarding selection of the proper size of a DLT, all studies have focused on the left-sided DLT in part because the right-sided DLT is used infrequently. A common problem with the left-sided DLT is the lack of objective guidelines to properly choose the correct or approximate size of DLT.

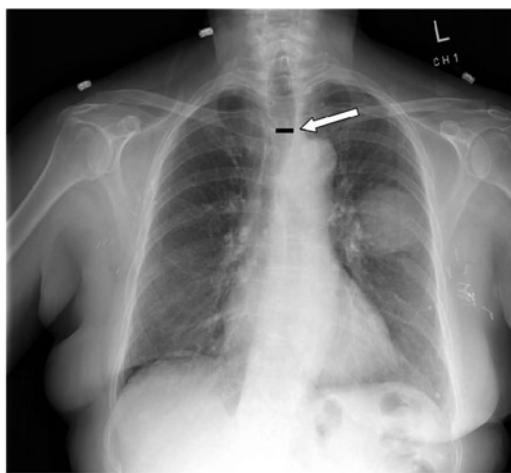
A left-sided DLT that is too small requires a large endobronchial cuff volume, which might increase the incidence of malposition. In addition, a small DLT does not readily allow fiberoptic bronchoscope placement and can make suction difficult. A properly sized DLT is one in which the main body of the tube passes without resistance through the glottis and advances easily within the trachea, and in which the bronchial component passes into the intended bronchus without difficulty. In a study performed in adult cadavers, it was shown that the cricoid ring diameter never exceeds the diameter of the glottis. If a DLT encounters resistance when passing the glottis, it is likely that the DLT would encounter resistance while passing the cricoid ring [11].

There are reports of complications related to the use of an undersized DLT. A tension pneumothorax and pneumomediastinum occurred after the endobronchial tip of an undersized DLT had migrated too far into the left lower bronchus, and the entire tidal volume was delivered into a single lobe [12]. Also, smaller DLTs might present with more resistance to gas flow and more intrinsic auto-positive end-expiratory pressure compared with the wider lumen of larger DLTs [13]. Airway-related complications have been reported with undersized left-sided DLTs. A rupture of the left mainstem bronchus by tracheal portion of a DLT has been reported

[14]. A longitudinal laceration of the left mainstem bronchus occurred. The cause of this complication was believed to be an undersized DLT, which allowed the endotracheal portion of the DLT to enter the left mainstem bronchus. In addition, an oversized DLT also can be associated with bronchial rupture in a small adult patient [15].

Brodsky et al. [16] reported that measurement of tracheal diameter at the level of the clavicle on the preoperative posteroanterior chest radiograph can be used to determine proper left-sided DLT size. These methods lead to a 90% increase in the use of larger left-sided DLTs (i.e., 41 F DLT in men and 39 F and 41 F DLT in women). However, a study involving Asian patients by Chow et al. [17], using the methodology of Brodsky et al. [16], found this approach less reliable. In the Chow et al. [17] study, the overall positive predictive value for the proper left size of a left-sided DLT was 77% for men and 45% for women. This method seems to have limited use in patients of smaller stature, such as women and people of Asian descent, and an alternative method should be sought, including placement of a different lung isolation device such as an independent bronchial blocker through a single-lumen endotracheal tube. Figure 16.1 shows the guidelines to predict the proper left-sided DLT based upon measurements of the tracheal width from the chest X-ray according to Brodsky et al. [16].

A recent study involving thoracic anesthesiologists by Amar et al. [18] has shown that the use of a smaller DLT (i.e., 35 F or



The arrow indicates the level of the clavicles. The black line indicates the width of the trachea.

Left Bronchocath Double-Lumen Endotracheal Tubes Guidelines		
Measured Tracheal Width (mm)	Predicted Left Bronchus Width (mm)	Recommended DLT size (F)
≥ 18	≥ 12.2	41
≥ 16	≥ 10.9	39
≥ 15	≥ 10.2	37
≥ 14	≥ 9.5	35

FIG. 16.1. Left bronchocath double lumen endotracheal tubes guideline. Modified from Brodsky et al. [16].

37 F left-sided DLT) rather than a conventionally large sized DLT (i.e., 39 or 41 F) was not associated with any difference in clinical intraoperative outcomes, regardless of patient size or gender in 300 patients undergoing thoracic surgery requiring lung isolation. However, in their study only 51 (35%) of the patients who received a 35 F DLT were males and 92 (65%) were females. In practice, women usually receive a 35 F DLT; therefore, the question of whether or not a 35 F for all patients is favorable remains unclear.

Another alternative that has been suggested in order to predict the proper size of a right-sided or left-sided DLT is a three-dimensional image reconstruction of tracheobronchial anatomy generated from spiral computed tomography (CT) scans combined with superimposed transparencies of DLTs [19]. Taken together, these studies suggest that chest radiographs and CT scans are valuable tools for selection of proper DLT size, in addition to their proven value in assessment of any abnormal tracheobronchial anatomy. These images should be reviewed before placement of a DLT. Particular emphasis should be made in viewing a posteroanterior chest radiograph in order to assess the shadow of tracheobronchial anatomy along with bronchial bifurcation. It is estimated that in 75% of the films the left mainstem bronchus shadow is seen. The trachea is located in the midline position, but often can be deviated to the right at the level of the aortic arch, with a greater degree of displacement in the setting of an atherosclerotic aorta, advanced age, or in the presence of severe chronic obstructive pulmonary disease (COPD). With COPD or aging, the lateral diameter of the trachea may decrease with an increase in the anteroposterior diameter. Conversely, COPD may also lead to softening of the tracheal rings with a decrease in the anteroposterior diameter of the trachea. The cricoid cartilage is the narrowest part of the trachea with an average diameter of 17 mm in men and 13 mm in women.

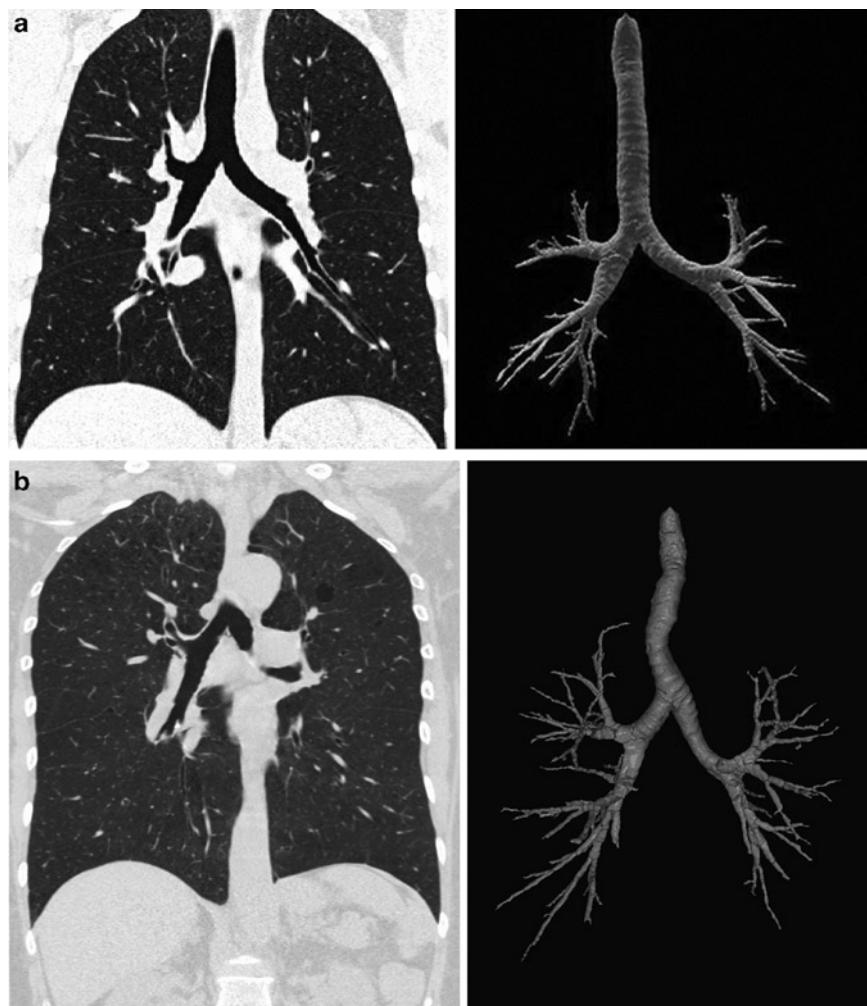
Figure 16.2a shows a multidetector three-dimensional CT scan of the chest displaying the trachea and bronchial anatomy in a 25-year-old healthy volunteer; Fig. 16.2b shows the changes that occur in a 60-year-old man with severe COPD, which shows a deviated trachea and narrow bronchus. Points of importance include the recognition of any distorted anatomy identified in the films prior to placement of DLTs.

Methods of Insertion

Two techniques are used most commonly by anesthesiologists when inserting and placing a DLT. The first is the blind technique, that is, when the DLT is passed with direct laryngoscopy, then turned to the left (for a left-sided DLT) or right (for a right-sided DLT) after the endobronchial cuff has passed beyond the vocal cords. The DLT then is advanced until the depth of insertion at the teeth is approximately 29 cm for both men and women if the patient's height is at least 170 cm [20].

The second technique employs fiberoptic bronchoscopy guidance, where the tip of the endobronchial lumen is guided

FIG. 16.2. (a) Male tracheobronchial tree via multidetector three-dimensional computer tomography scan in a healthy 25 year old. (b) Male tracheobronchial tree via multidetector three-dimensional computer tomography scan in a 60 year old with chronic obstructive pulmonary disease (COPD) [29].



after the DLT passes the vocal cords; direction is sought with the aid of a flexible fiberoptic bronchoscope. A study by Boucek et al. [21] comparing the blind technique versus the fiberoptic bronchoscopy-guided technique showed that of the 32 patients who underwent the blind technique approach, primary success occurred in 30 patients. In contrast, in the 27 patients receiving the bronchoscopy-guided technique, primary success was achieved only in 21 patients and eventual success in 25 patients. This study also showed that the time spent placing a DLT was an average of 88 s for the blind technique and 181 s for the directed bronchoscopic approach. Although both methods resulted in successful left mainstem bronchus placement in most patients, more time was required when the fiberoptic bronchoscopy guidance technique was used. In addition, two patients in each group required an alternative method for tube placement. Either method may fail when used alone. Figure 16.3 shows the blind method technique and Fig. 16.4 shows a fiberoptic bronchoscopy guidance technique for placement of a left-sided DLT.

Right-Sided Double-Lumen Endotracheal Tubes

Although a left-sided DLT is used more commonly for most elective thoracic procedures [22], there are specific clinical situations in which the use of a right-sided DLT is indicated. Table 16.3 displays the indications for use of a right-sided DLT.

The anatomic differences between the right and left mainstem bronchus are reflected in fundamentally different designs of the right-sided and left-sided DLTs. Because the right mainstem bronchus is shorter than the left bronchus and because the right upper lobe bronchus originates at a distance of 1.5–2 cm from the carina, techniques using right endobronchial intubation must take into account the location and potential obstruction of the orifice of the right upper lobe bronchus. The right-sided DLT incorporates a modified cuff, or slot, on the endobronchial side that allows ventilation of the right upper lobe. Figure 16.5 displays the Sheridan and the Mallickrodt right-sided DLTs.

FIG. 16.3. Blind technique for placement of a left-sided DLT [63].

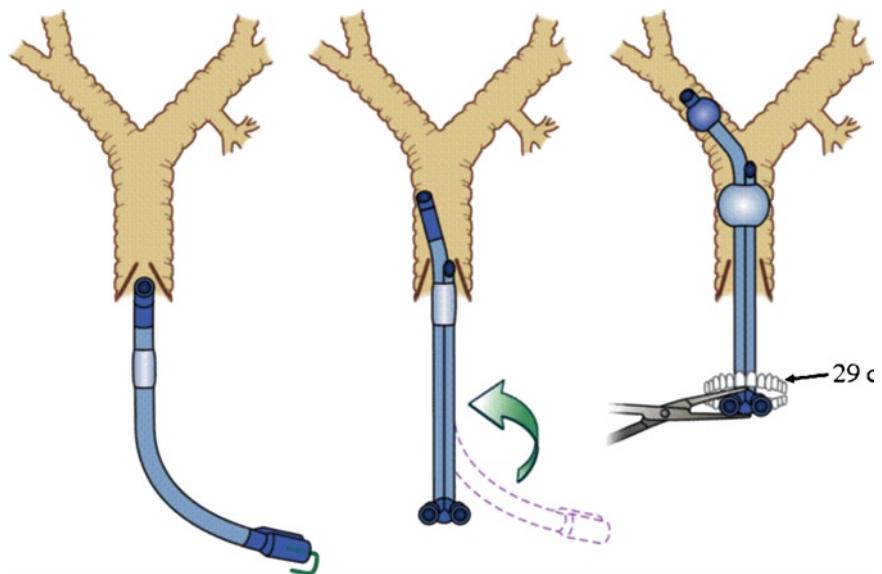


FIG. 16.4. Shows a fiberoptic bronchoscopy guidance technique for placing a left-sided DLT [63].

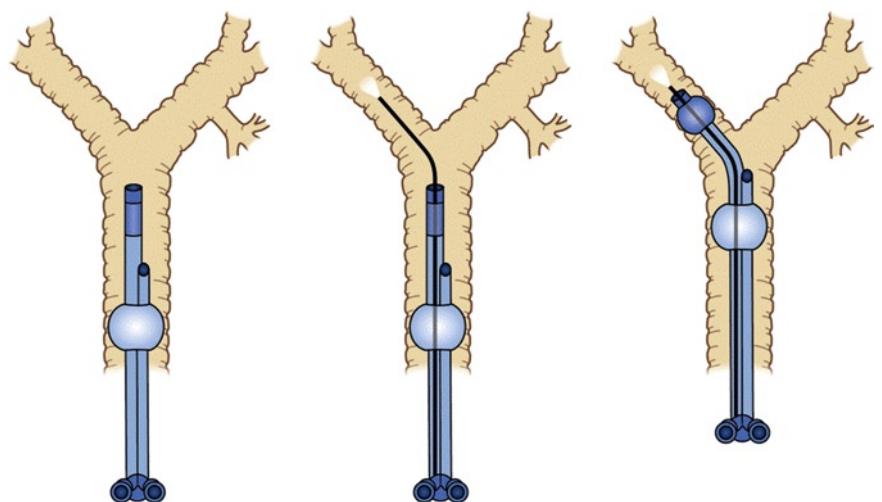


TABLE 16.3. Indications for a right-sided DLT.

- Any contraindication to placement of a left-sided DLT
- Distorted anatomy of the entrance of left mainstem bronchus by an intra-bronchial or external compression
- Compression of the entrance of the left mainstem bronchus due to a descending thoracic aortic aneurysm
- Left lung transplantation
- Left-sided sleeve resection
- Left-sided pneumonectomy

Safety

In theory, the left-sided DLT and right-sided DLT should be equally safe and efficacious for collapse of either the right or the left lung. In practice, however, use of the right-sided DLT has become controversial. An early study showed that

because of bronchial anatomy, the left-sided DLT is simpler to use and has a greater margin of safety than the right-sided DLT [23]. Another study [24] has shown failure to ventilate the right upper lobe in 11% of patients and obstruction of the right upper bronchus in 89% of patients after right-sided DLT placement; studies relying on fiberoptic bronchoscopy guidance techniques have shown no increased risk of obstruction of the right upper lobe orifice [25]. A right-sided DLT from the Mallinckrodt brand has been modified to increase the margin of safety. In this right-sided Broncho-Cath® DLT, the opening slot of the ventilating orifice for the right upper bronchus lobe has been widened and consists of an enlarged area of the lateral orifice; this modification has increased the alignment between the opening slot and the right upper lobe bronchus [26]. A contraindication for right-sided DLT use is the presence of an anomalous right upper lobe takeoff from

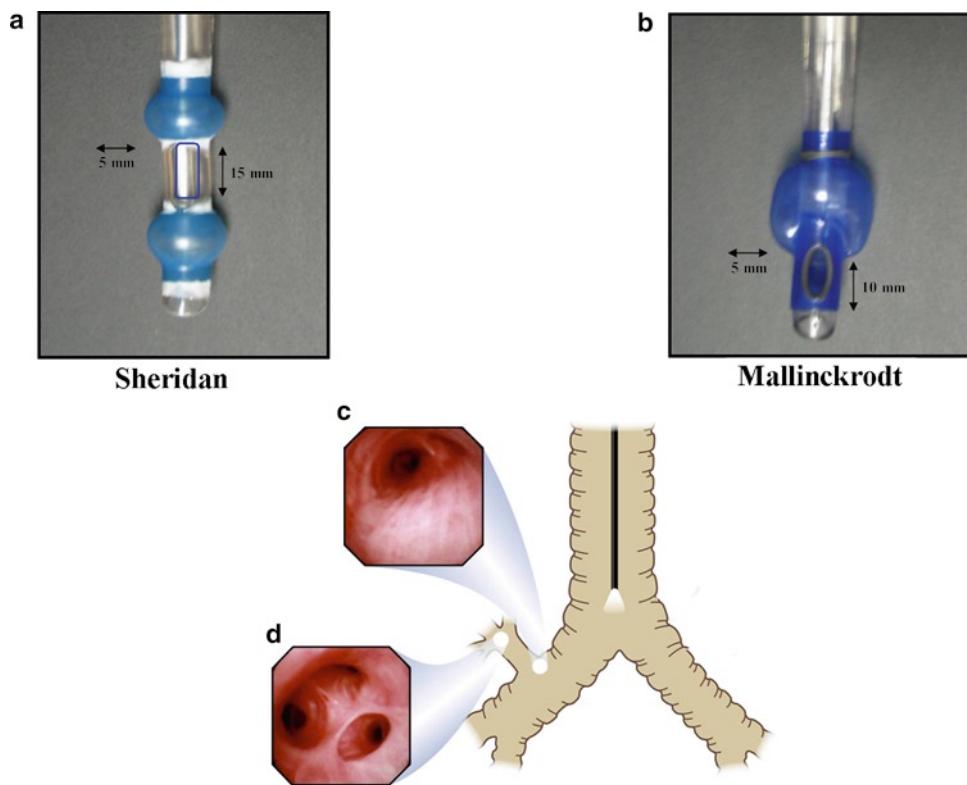


FIG. 16.5. (a) Sheridan right-sided DLT. (b) Mallinckrodt right-sided DLT. (c) View of the right mainstem bronchus showing the bronchus intermedius towards the center of the photo and the smaller right upper lobe orifice to the right. (d) The three segments of the right upper lobe (the “clover-leaf” view).

the trachea, which has been estimated to be present in 1 of 250 otherwise normal subjects [27]. A recent study involving the use of right- or left-sided DLTs has shown that these have identical clinical performances. In this study, the authors hypothesized that placing a left-sided DLT for a right-sided lung isolation; the tubes will have similar performance. This retrospective study reported no difference in the incidence of duration of hypoxemia hypercarbia or high airway pressures [28]. Unfortunately, this study was retrospective in nature, and also the authors showed greater than 35 cm H₂O of peak inspiratory pressure in over 65% of the cases reported in both groups during OLV.

Placement Technique

The preferred technique for placement of a right-sided DLT is with the fiberoptic bronchoscopy guidance technique. After the right-sided DLT is passed beyond the vocal cords under direct laryngoscopy, the fiberoptic bronchoscope is advanced through the endobronchial lumen. Before advancing the DLT, the tracheal carina, the entrance of the right mainstem bronchus, and the entrance of the right-upper lobe bronchus are identified. Then the DLT is rotated 90° to the right and advanced with the aid of the fiberoptic bronchoscope. The optimal position of a right-sided DLT is one that provides

good alignment between the opening slot of the endobronchial lumen in relationship to the entrance of the right-upper lobe bronchus and, distally, a clear view of the bronchus intermedius and the right lower lobe bronchus seen from the endobronchial lumen. From the tracheal view, the optimal position for a right-sided DLT provides a view of the edge of the blue cuff of the endobronchial balloon when inflated just below tracheal carina and a view of the entrance of the right mainstem bronchus [29]. Figure 16.6 shows the optimal position of a right-sided DLT seen from the endobronchial or endotracheal view with a fiberoptic bronchoscope.

Left-Sided Double-Lumen Endotracheal Tubes

Placement Technique

Placement and positioning of a left-sided DLT can be accomplished with either technique discussed earlier, the blind technique in which the left-sided DLT is passed beyond the vocal cords (endobronchial cuff) and the tube is rotated 90° counterclockwise and advances until the tip of the tube enters the left mainstem bronchus, or the bronchoscopy guidance technique, in which the endobronchial tip is passed beyond the

FIG. 16.6. Optimal position of a right-sided DLT. (a) The view of the right upper lobe through the ventilating side slot of the bronchial lumen. (b) The view from the tracheal lumen of the main carina with the bronchial lumen in the right mainstem bronchus [29].

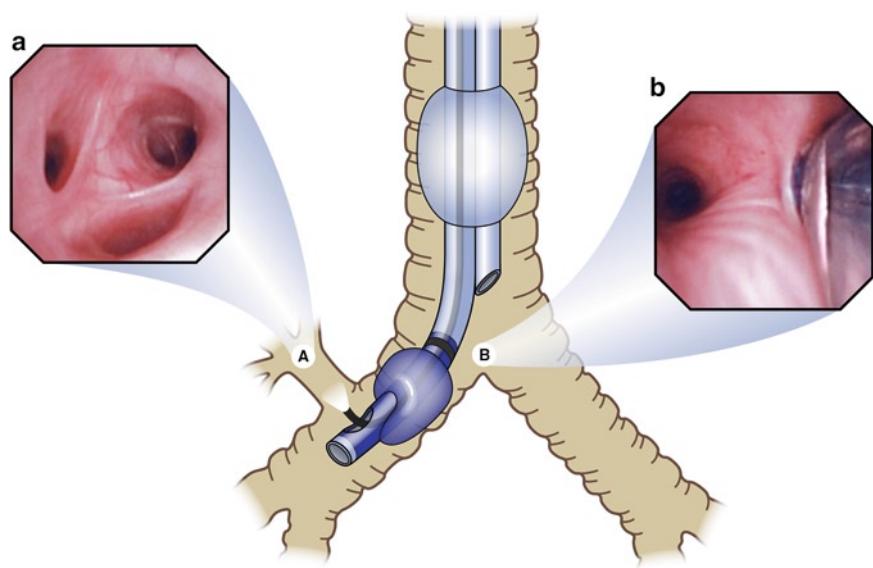
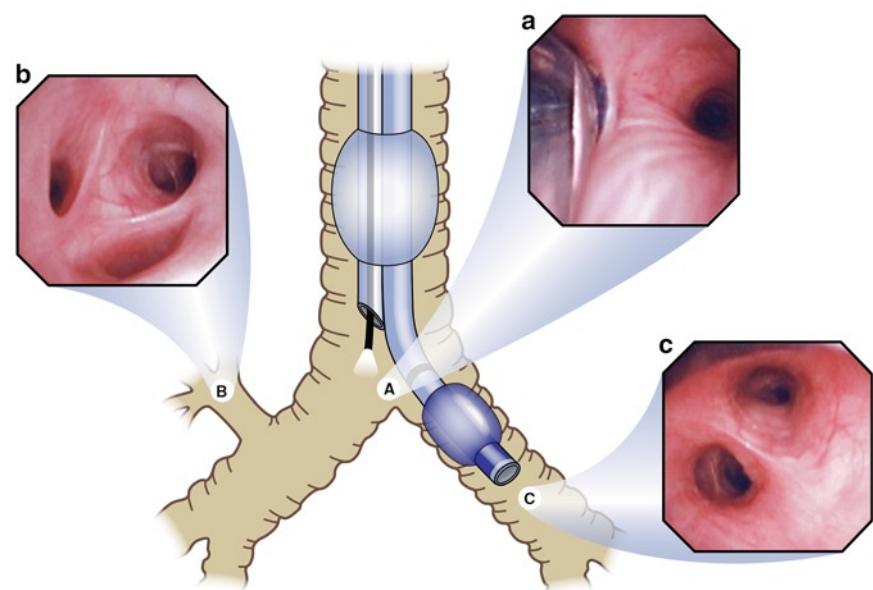


FIG. 16.7. The optimal position of a left-sided DLT. (a) View from the tracheal lumen of the unobstructed entrance of the right mainstem bronchus. (b) View from the tracheal lumen of the right-upper bronchus. (c) View from the bronchial lumen of the left-upper (above) and left-lower (below) lobe bronchi [29].



vocal cords and guided through the trachea with the aid of the fiberoptic bronchoscope until the entrance of the left mainstem bronchus is identified and the tube is introduced into the left bronchus. The optimal position for a left-sided DLT as seen with the fiberoptic bronchoscope is the one that allows, from the tracheal lumen view, observation of a fully inflated endobronchial cuff with no more than 3 mL of air located 5–10 mm below the tracheal carina inside the left mainstem bronchus. The second important view is the endobronchial bronchoscopy view. Two observations are relevant: first, the fiberoptic bronchoscope is advanced inside the endobronchial lumen, and the patency of the lumen is observed before advancing the bronchoscope through the blue portion of the tube; the second view is at the distal end of the endobronchial

tip of the tube, where a clear and unobstructed view of the left-upper and lower lobe bronchus entrance orifices are visualized distally. In order to recognize the right mainstem bronchus while placing a left-sided DLT, the fiberoptic bronchoscope is advanced through the tracheal lumen below the main tracheal carina to the right side approximately 1–2 cm at which the point the orifice of the right-upper lobe bronchus is seen at 3–4 o'clock on the lateral wall. Advancing the fiberoptic bronchoscope inside this orifice should provide a clear view of the apical, anterior, and posterior segments (the “clover-leaf” view). This is the only structure in the tracheobronchial tree that has three orifices. Figure 16.7 shows the optimal position of a left-sided DLT as seen with a fiberoptic bronchoscope.

Auscultation and Fiberoptic Bronchoscopy when Placing Double-Lumen Endotracheal Tubes

Evidence strongly suggests that auscultation alone is unreliable for confirmation of proper DLT placement. However, the basic principle of auscultation and clamping maneuvers while testing the proper placement of a DLT must be routinely applied prior to the use of fiberoptic bronchoscopy. For a left-sided DLT, the endobronchial lumen should be placed below the tracheal carina into the left mainstem bronchus and the depth of the tube in a 170 cm tall subject should be approximately 29 cm at the level of the teeth. Clamping the limb connector of the tracheal lumen should reveal absence of breath sounds on the right side of the chest (right hemithorax). After this maneuver is completed, the next step is to ventilate both lungs then to clamp the limb connector of the endobronchial lumen should reveal absence of breath sounds on the left side of the chest (left hemithorax). If none of these maneuvers are successful, or confusion ensues with breath sounds and the location of the DLT, a fiberoptic bronchoscopy exam takes precedent. A study involving 200 patients who were intubated by the blind technique in whom confirmation of placement of DLTs was done first with auscultation and clamping one of the ports of the connector of the DLT and with a second anesthesiologist with expertise in fiberoptic bronchoscopy reconfirming the placement of the DLT showed that 35% of the tubes placed were malpositioned when auscultation was used alone. All detected malpositions were eventually corrected [30]. A study by Brodsky and Lemmens [22] reported their clinical experience with the use of left-sided DLTs. Using auscultation and clinical signs, they reported 98% efficacy in lung collapse, yet in only 58 instances they used fiberoptic bronchoscopy to attempt to place the DLTs correctly. In this study, there were 71 patients (6.2%) in whom the DLT was found not to be in a satisfactory position, requiring readjustment after initial placement. What is important from the Brodsky study [22] is the fact that

in 56 patients the DLT was considered too deep into the left bronchus, and indirectly this was a cause of hypoxemia in 21 of 56 patients who had a malpositioned tube. Anesthesiologists should be able to avoid this complication with the use of fiberoptic bronchoscope. In a report related to the national confidential inquiry into perioperative deaths in Great Britain [31], which detailed the management of patients undergoing esophagogastrectomy, it was shown that 30% of deaths reported were associated with malposition of DLTs. The problems ranged from use of multiple DLTs to prolonged periods of hypoxia and hypoventilation. The anesthesiologists did not use a fiberoptic bronchoscope to confirm DLT position before surgery, during surgery, or when the DLT was placed incorrectly [32].

In another report from Great Britain, Seymour [33] reported a survey among anesthesiologists in a single institution, in which they participated in 506 placements of left- or right-sided DLTs; in their report, only 56% of the cases managed used fiberoptic bronchoscopy to confirm the proper placement of the DLTs. In more than 10% of their cases, hypoxemia was present in the intraoperative period. An editorial by Slinger [34] pointed out the importance of using fiberoptic bronchoscopy to confirm placement of DLTs.

A study involving nonthoracic anesthesiologists with very limited experience in lung separation techniques showed that when placing lung isolation devices (DLTs or bronchial blockers) there was a 38% incidence in unrecognized malpositions when these devices were placed with the fiberoptic bronchoscope. The possible causes were lack of skill with fiberoptic bronchoscopy and lack of recognition of the tracheobronchial anatomy [35]. It is the author's opinion that fiberoptic bronchoscopy is essential and mandatory to achieve 100% success in placement and positioning of DLTs as long as the anesthesiologist is able to recognize proper tracheobronchial anatomy and has skills with flexible fiberoptic bronchoscopy. Table 16.4 displays the findings and outcomes when auscultation, clamping maneuvers, and or fiberoptic bronchoscopy were used to position and achieve optimal position of the DLTs.

TABLE 16.4. Role of auscultation, fiberoptic bronchoscopy, and/or both during lung isolation.

References	Number of patients	Method	Outcome
Brodsky and Lemmens [22]	1,170 DLTs (retrospective study)	Clinical experience over 8-year period (1993–2001) Auscultation and clinical signs	Successful lung isolation 98% 56 DLT too deep in the left bronchus (<i>n</i> =21 hypoxemia)
Klein et al. [30]	200 L-R DLT's (prospective study)	Auscultation/clamping/followed by a fiberoptic bronchoscopy with a second	Fiberoptic bronchoscopy was used <i>n</i> =58 35% malpositions Optimal position achieved with the use of fiberoptic bronchoscopy in all cases
Seymour et al. [33]	506 L-R DLTs (survey)	Audit of DLT Auscultation/clamping maneuvers or fiberoptic bronchoscopy	56% used fiberoptic bronchoscopy >10% hypoxemia ($\text{SpO}_2 < 88\%$)

DLT double-lumen endotracheal tube; R right; L left

New Technology with Double-Lumen Endotracheal Tubes

Fuji Systems in Tokyo, Japan has introduced the Silbroncho DLT, which is made of silicone. The unique characteristic of this device relies on the wire-reinforced endobronchial tip. Also, the short bronchial tip and reduced bronchial cuff should increase the margin of safety when compared with a Bronchocath left-sided DLT. At the present time, only a left-sided Silbroncho DLT is available on the market [36]. Its effectiveness has not been reported.

Also, there is a newly designed right-sided DLT, the Cliny® (Create Medic Co., Ltd, Yokohama, Japan). This device has a long oblique bronchial cuff and two ventilation slots for the right-upper lobe. The proximal part of the bronchial cuff is located immediately opposite the tracheal orifice. This device can be useful in patients with a very short right mainstem bronchus [37]. Figure 16.8a displays the Silbroncho left-sided DLT and (b) displays the Cliny® right-sided DLT.

Another newly designed DLT has been designed to enable rapid and reliable lung isolation using a bronchial blocker. The Papworth BiVent Tube [38, 39] is a DLT with two D-shaped lumens arranged in a side-by-side configuration, separated by a central position. The tube characteristics include a preformed single posterior concavity and a single inflatable, low-volume, high-pressure tracheal cuff. At the distal end, there are two pliable crescent-shaped flanges arising from the central position to form a forked tip. The purpose of the forked tip is to seat

at the tracheal carina. A bronchial blocker can be advanced blindly through either lumen and is guided into a bronchus. The size available for the Papworth BiVent tube at the present time is 43 F. According to the developers, the Papworth BiVent tube can be used without the requirement for endoscopic guidance. Unfortunately, at the present time there are no studies in humans to confirm its clinical use during lung separation.

Complications Associated with Double-Lumen Endotracheal Tube Placement

The most common problems and complications from the use of DLTs are malpositions and airway trauma. A malpositioned DLT fails to allow collapse of the lung, causing gas trapping during positive pressure ventilation, or it may partially collapse the ventilated or dependant lung, producing hypoxemia. A common cause of malposition is dislodgement of the endobronchial cuff because of overinflation, surgical manipulation of the bronchus, or extension of the head and neck during or after patient positioning [40].

Airway trauma and rupture of the membranous part of the trachea or the bronchus continue to be infrequent problems with the use of DLTs [14, 15]. These complications can occur during insertion and placement, while the case is in progress, or during extubation [41–43]. Another problem that has been reported is the development of bilateral pneumothoraces or a tension pneumothorax in the dependent, ventilated lung [44, 45]. A 25-year review of the literature by Fitzmaurice and Brodsky [46] found that most airway injuries were associated with undersized DLTs, particularly in women who received a 35 F or 37 F disposable DLT. It is likely that airway damage occurs when an undersized DLT migrates distally into the bronchus and the main tracheal body of the DLT advances into the bronchus, producing lacerations or rupture of the airway. Airway damage during the use of DLTs can present as unexpected air leaks, subcutaneous emphysema, massive bleeding into the lumen of the DLT, or protrusion of the endotracheal or endobronchial cuff into the surgical field, with visualization of this by the surgeon. If any of the aforementioned problems occur, a bronchoscopic examination should be performed and surgical repair performed.

Benign complications with the use of the DLT have been reported by Knoll et al [47]. In their comparative study between the DLT and the endobronchial blocker, the development of postoperative hoarseness occurred significantly more commonly in the DLT group when compared to the endobronchial blocker group; however, the incidence of bronchial injuries was comparable between groups.

Bronchial Blockers

An alternative method to achieve lung separation involves blockade of a mainstem bronchus to allow lung collapse distal to the occlusion [4]. Bronchial blockers also can be used

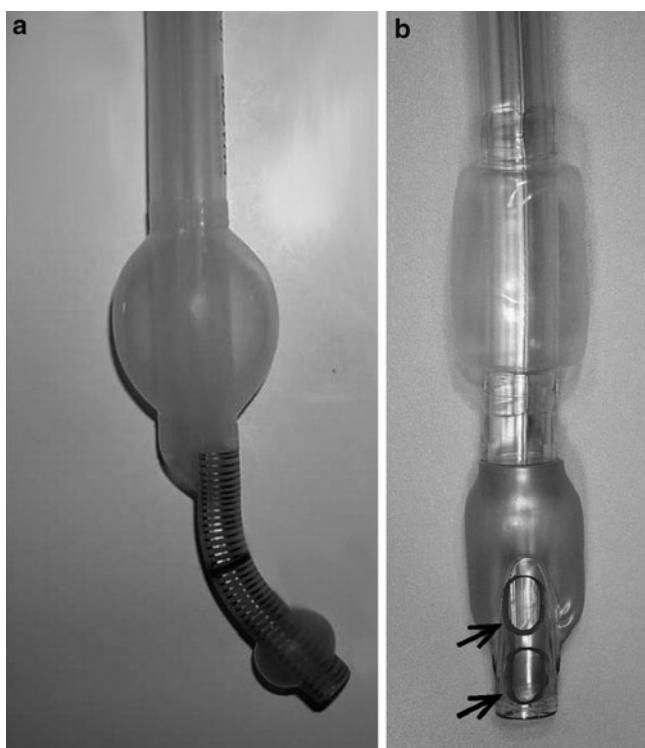


FIG. 16.8. (a) Silbroncho left-sided DLT. (b) Cliny® right-sided DLT.

selectively to achieve lobar collapse, if needed [48–54]. Currently, there are different bronchial blockers available to facilitate lung separation collapse; these devices either are attached to a single-lumen endotracheal tube with an enclosed bronchial blocker (Torque Control Blocker Univent) [4] or are used independently through or alongside a conventional single-lumen endotracheal tube, such as the wire-guided endobronchial blocker Arndt® blocker [6], the Cohen tip-deflecting endobronchial blocker [7], or the Fuji Uniblocker® [8, 55].

Torque Control Blocker Univent

The Univent® tube consists of a single-lumen endotracheal tube with an enclosed and movable bronchial blocker made of flexible, nonlatex material, and it includes a flexible shaft that is easier to guide into a bronchus [5]. The bronchial balloon has a high-pressure, low-volume cuff that requires approximately 2 mL of air to produce an airtight seal if selective lobar blockade is used or 4–8 mL of air if the total blockade of the bronchus is desired. The bronchial blocker has a 2-mm diameter lumen that can be used for suctioning or for oxygen administration and it should be closed before insertion. One of the advantages of the Univent® blocker is its utility in patients in whom the airway is considered difficult for direct laryngoscopy and during unanticipated difficult endotracheal intubation [56–62].

Placement of the Univent® blocker is straightforward. First the bronchial blocker is lubricated to facilitate passage. The enclosed bronchial blocker is fully retracted into the lumen of the tube. Conventional endotracheal tube placement is performed via direct laryngoscopy, and then a fiberoptic bronchoscope is passed through a Portex swivel adaptor into the endotracheal tube. Under direct vision, the enclosed bronchial blocker is advanced into the targeted bronchus. All bronchial blockers must be directed into the bronchus of the surgical side, where the lung collapse is to occur.

Independent Bronchial Blockers During Lung Isolation

Another alternative to achieve lung separation is by using an independent blocker passed through an in situ single-lumen endotracheal tube. The various devices considered to be independent blockers include the wire-guided endobronchial blocker (Arndt® blocker), the Cohen tip-deflecting endobronchial blocker, and the Fuji Uniblocker® [8, 55] (see Fig. 16.9).

Arndt® Wire-Guided Endobronchial Blocker

The Arndt® blocker [6] is an independent blocker attached to a 5 F, 7 F, or 9 F catheter that is available in 65- and 78-cm lengths with an inner lumen that measures 1.4 mm in diameter. Near the distal end of the catheter, side holes are incorporated to facilitate lung deflation. These side holes are present only in the 9 F Arndt® block. The Arndt® blocker has a high-volume, low-pressure cuff with either an elliptical or spherical shape (see Fig. 16.10). A unique feature of the Arndt®



FIG. 16.9. Three independent bronchial blockers currently available in North America (see Table 16.5 for details). *Left:* The Cohen® Tip-Deflecting Endobronchial Blocker 9F (Cook Critical Care, Bloomington, IN), which allows anesthesiologists to establish single-lung ventilation by directing its flexible tip left or right into the desired bronchus using a control wheel device on the proximal end of the blocker in combination with fiberoptic bronchoscope (FOB) guidance. *Middle:* The Fuji Uniblocker®, 9F (Fuji Corp., Tokyo, Japan). It has a fixed distal curve that allows it to be rotated for manipulation into position with FOB guidance. Unlike its predecessor, the Univent, the Uniblocker is used with a standard endotracheal tube. *Right:* The wire-guided endobronchial blocker (Arndt® bronchial blocker; Cook Critical Care) introduced in 1999. It contains a wire loop in the inner lumen; when used as a snare over a FOB, it allows directed placement. The loop is then removed, and the 1.4-mm lumen may be used as a suction channel or for oxygen insufflation.



FIG. 16.10. The recently introduced Arndt® spherical bronchial blocker cuff (Cook Critical Care, Bloomington, IN). Some clinicians prefer to use this spherical cuff for right-sided surgery versus the original elliptical cuff because of the short length of the right mainstem bronchus.

blocker compared with other blockers is that the inner lumen contains a flexible nylon wire passing through the proximal end of the catheter and extending to the distal end, which exits as a small flexible wire loop. This blocker comes with a multiport connector. The wire loop of the Arndt® blocker is coupled with the fiberoptic bronchoscope and serves as a guide wire to introduce the blocker into the bronchus [63]. For the Arndt® blocker to function properly and allow manipulation with the adult fiberoptic bronchoscope, the proper size endotracheal tube must be used. For a 7 F blocker which can be used for a 40-kg patient, a 7.5-mm internal diameter (ID) single-lumen endotracheal tube is used, and for the larger 9 F Arndt® blocker, at least an 8.0-mm ID single-lumen endotracheal tube is used. Figure 16.11 displays the placement of an Arndt® blocker through a single-lumen endotracheal tube with the fiberoptic bronchoscope advanced through the guide wire loop.

The advantages of the Arndt® blocker include its use in patients who are already tracheally intubated [64], who present a difficult airway and require an awake orotracheal or nasotracheal intubation [65], or who require OLV during acute

trauma to the chest [66, 67]. In addition, an Arndt® blocker can be used as a selective lobar blocker in patients with previous pneumonectomy who require selective one-lobe ventilation [68] or as a selective blocker during severe pulmonary bleeding [69]. Figure 16.12 displays the use of a bronchial blocker for selective lobar blockade.

Methods of Placement

The Arndt® blocker is an independent endobronchial blocker that is passed through an existing single-lumen endotracheal tube. To facilitate insertion through the endotracheal tube, the blocker and the fiberoptic bronchoscope are lubricated. For a right-sided mainstem bronchus intubation, the spherically shaped blocker is recommended; for the left mainstem bronchus intubation, the elliptical or the spherical blocker is used.

The placement of the Arndt® blocker involves placing the endobronchial blocker through the endotracheal tube and using the fiberoptic bronchoscope and wire-guided loop to direct the blocker into a mainstem bronchus. The fiberoptic bronchoscope has to be advanced distally enough so that the

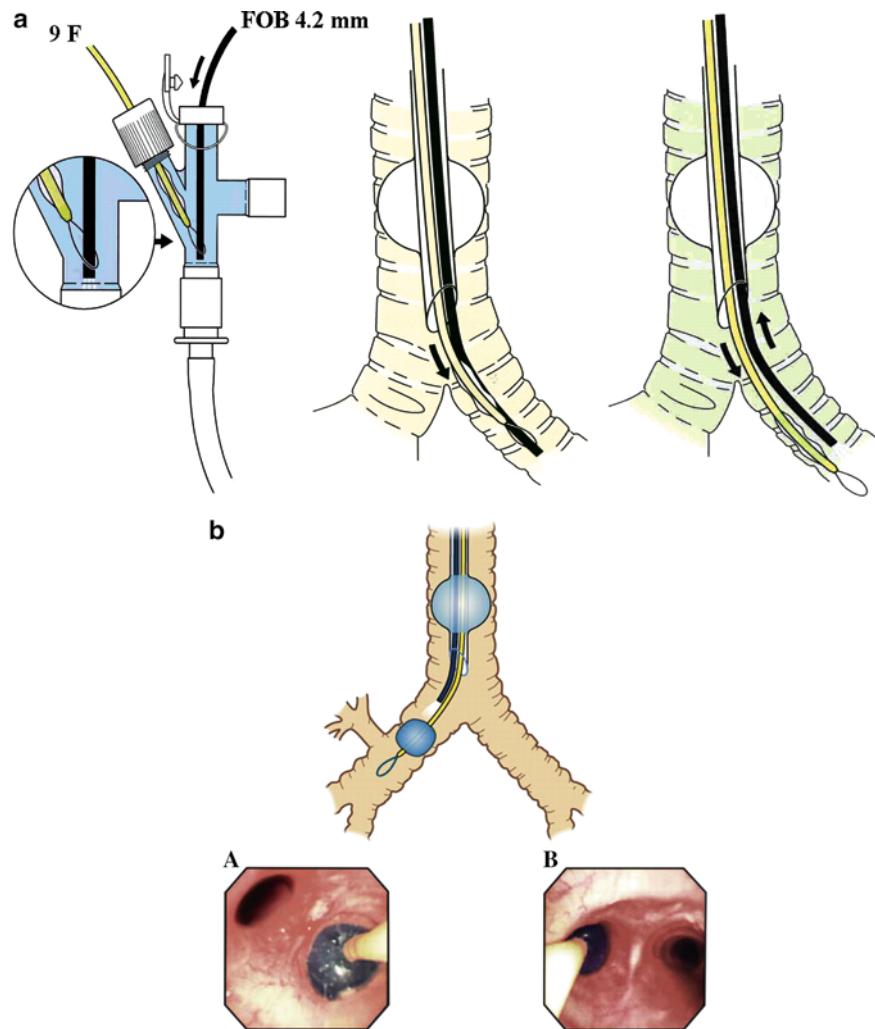


FIG. 16.11. (a) Placement of an Arndt® blocker through a single-lumen endotracheal tube with the fiberoptic bronchoscope advanced through the guide wire loop. (b) Optimal position of a bronchial blocker in the right or left mainstem bronchus as seen with a fiberoptic bronchoscope. A right mainstem blocker; B left mainstem blocker [63].

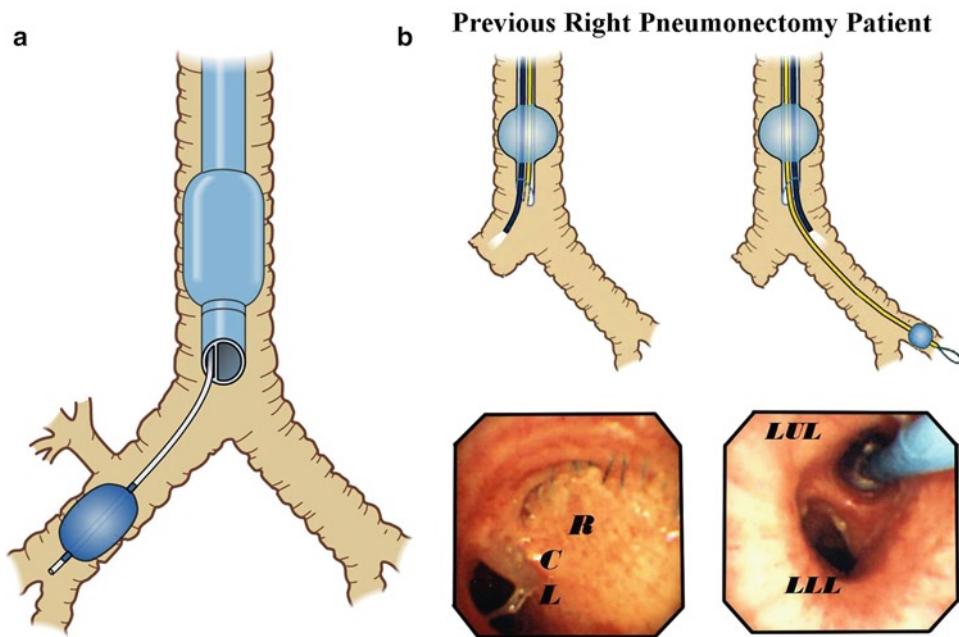


FIG. 16.12. (a) Selective lobar blockade where the blocker is sealing the right bronchus intermedius. (b) Patient with a previous right pneumonectomy where selective lobar blockade is used to occlude the left upper lobe. *R* stump of right mainstem bronchus; *C* main carina; *L* left mainstem bronchus; *LUL* left upper lobe; *LLL* left lower lobe [54].

Arndt® blocker enters the bronchus while it is being advanced. When the deflated cuff is beyond the entrance of the bronchus, the fiberoptic bronchoscope is withdrawn, and the cuff is fully inflated with fiberoptic visualization with 4–8 mL of air to obtain total bronchial blockade.

For right mainstem bronchus blockade, the Arndt® blocker can be advanced independently of the wire loop by observing its entrance into the right mainstem bronchus under fiberoptic visualization. Before turning the patient into a lateral decubitus position, the cuff of the blocker should be deflated, then advanced 1 cm deeper to avoid proximal dislodgement while changing the patient's position; the placement again is confirmed in the lateral decubitus position. The wire loop can be withdrawn to convert the 1.4-mm channel into a suction port to expedite lung collapse. The newest version of the Arndt® blocker has a cone-shaped device that is attached to the center channel to connect and facilitate suction [70, 71]. It is important to remove the wire loop to avoid inclusion in the stapling line of the bronchus [72]. The optimal position of the Arndt® blocker in the left or in the right bronchus is achieved when the blocker balloon's outer surface is seen with the fiberoptic bronchoscope at least 5 mm below the tracheal carina on the targeted bronchus and the proper seal is obtained.

Cohen® Flexitip Endobronchial Blocker

The Cohen® blocker is an independent endobronchial blocker that is available only in size 9 F and 65-cm length with an inner lumen measuring 1.4 mm in diameter. This device comes with

a spherically shaped balloon. Near the distal end of the catheter, there are side holes incorporated to facilitate lung deflation. This bronchial blocker has a high-volume, low-pressure cuff. The Cohen® blocker relies on a wheel-turning device located in the most proximal part of the unit that allows deflection of the tip of the distal part of the blocker into the desired bronchus [2, 7]. This device has been purposely preangled at the distal tip to facilitate insertion into a target bronchus. Also, there is a torque grip located at the 55-cm mark to allow rotating the blocker. In the distal tip above the balloon, there is an arrow that when seen with the fiberoptic bronchoscope indicates in which direction the tip deflects. This Cohen® blocker also comes with a multiport adaptor to facilitate an airtight seal when in place. The indications for use of the Cohen® blocker are the same as for the Arndt® blocker. Figure 16.13 displays the Cohen® blocker.

Methods of Placement

The Cohen® blocker is advanced through an 8.0-mm ID single-lumen endotracheal tube; before insertion, the blocker balloon is tested and then fully deflated. This blocker needs to be lubricated to facilitate insertion and passage through the single-lumen endotracheal tube.

The placement of the Cohen® blocker involves placing the endobronchial blocker through the endotracheal tube and using the fiberoptic bronchoscope to observe the direction of the blocker into a mainstem bronchus. For blocking the right mainstem bronchus, the optimal position is the one that provides

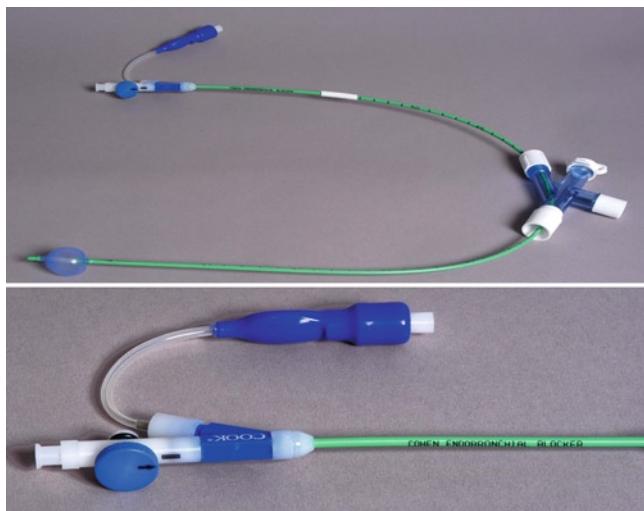


FIG. 16.13. The Cohen flexitip bronchial blocker with a multiport connector [7].

a view of the outer surface of the fully inflated balloon (4–8 mL of air) with the fiberoptic bronchoscope at least 5 mm below the tracheal carina on the right mainstem bronchus.

Intubation of the left mainstem bronchus can be facilitated by allowing the tip of the single-lumen endotracheal tube to be near the entrance of the left bronchus, then twisting the Cohen® blocker to the left side. After the blocker is seen inside the left bronchus, the single-lumen endotracheal tube is withdrawn a few centimeters. A different alternative is to turn the head towards the right allowing the left main bronchus to displace to the midline. This maneuver will facilitate the placement of a Cohen® blocker into the left mainstem bronchus. The optimal position in the left mainstem bronchus is achieved when the blocker balloon's outer surface is seen with the fiberoptic bronchoscope at least 5 mm below the trachea carina inside the left mainstem bronchus.

Fuji Uniblocker®

The Fuji Uniblocker® is an independent bronchial blocker that is available in 4.5 F and 9 F size and is 65 cm in length that

has a high-volume balloon made of silicone with a gas barrier property to reduce diffusion of gas into or out of the cuff. Also, with its maximal cuff inflation of 6 mL of air, this new bronchial blocker's transmitted pressure tested in vitro was <30 mmHg, which does not exceed the recommended safety limit in relationship to bronchial mucosa [73]. In addition, the Fuji Uniblocker® is equipped with a swivel connector. The swivel connector allows easy insertion of the fiberoptic bronchoscope. The Fuji Uniblocker® has a torque-control blocker with an incorporated shaft that allows the guidance through the desired bronchus. A recent study [8] involving the use of the Fuji Uniblocker® compared with the Arndt® and Cohen® blocker showed that surgical exposure was clinically equivalent to left-sided DLTs for thoracoscopic or open thoracotomies; however, the bronchial blockers including the Fuji Uniblocker® took a longer time to position and required more intraoperative repositioning when compared to left-sided DLTs. Another report [74], this one examining the use Fuji Uniblocker® in patients undergoing thoracoscopic surgery, showed a better quality of lung collapse with left-sided procedures than right-sided procedures. The indications for use of the Fuji Uniblocker® are the same as for the Arndt® blocker. Table 16.5 displays the characteristics of the Arndt® blocker, the Cohen® Flexitip Endobronchial Blocker, and the Fuji Uniblocker®. The Cohen® and Fuji® blockers can be easily placed through the glottis or tracheostomy external to an endotracheal tube, if required in small patients, and the blocker position confirmed with a FOB passed through the endotracheal tube.

Methods of Placement

The Fuji Uniblocker® size 9 F is advanced through an 8.0-mm ID single-lumen endotracheal tube; before insertion the blocker balloon is tested, and then fully deflated. This blocker needs to be lubricated to facilitate insertion and passage through the single-lumen endotracheal tube.

The placement of the Fuji Uniblocker® involves placing the endobronchial blocker through the endotracheal tube and using the fiberoptic bronchoscope to observe the direction of the blocker into a mainstem bronchus. The torque control shaft with the blocker allows guidance into the desired target bronchus. For blocking the right mainstem bronchus, the optimal

TABLE 16.5. Characteristics of the Arndt® blocker, the Cohen® flexitip endobronchial blocker, and the Fuji Uniblocker®.

	Cohen blocker	Arndt® blocker	Fuji Uniblocker®
Size	9 F	5 F, 7 F, and 9 F	4.5 F, 9 F
Balloon shape	Spherical	Spherical or elliptical	Spherical
Guidance mechanism	Wheel device to deflect the tip	Nylon wire loop that is coupled with the fiberoptic bronchoscope	None, preshaped tip
Smallest recommended *ETT for coaxial use	9 F (8.0 ETT)	5 F (4.5 ETT), 7 F (7.0 ETT), 9 F (8.0 ETT)	4.5 F (4.5 ETT) 9 F (8.0 ETT)
Murphy eye	Present	Present in 9F	Not present
Center channel	1.6-mm internal diameter	1.4-mm internal diameter	2.0-mm internal diameter

Reprinted from Campos [55], with permission

ETT single endotracheal tube

position is the one that provides a view of the outer surface of the fully inflated balloon (4–8 mL of air) with the fiberoptic bronchoscope at least 5 mm below the tracheal carina on the right mainstem bronchus. The optimal position in the left mainstem bronchus is achieved when the blocker balloon's outer surface is seen with the fiberoptic bronchoscope at least 5–10 mm below the trachea carina inside the left mainstem bronchus.

Complications with the Use of Bronchial Blockers

Although serious complications have been reported with the use of current bronchial blockers, these complications appear to be more benign than those involving DLTs. A structural complication has been reported in the torque-control Univent blocker in which a fracture of the blocker cap connector occurred in 2 of the first 50 tubes used [75]. Failure to achieve lung separation because of abnormal anatomy, in which the entrance of the right-upper lobe bronchus was located above the tracheal carina, or lack of seal within the bronchus, also has been reported [76, 77]. Inclusion of the enclosed bronchial blocker into the stapling line has been reported during a right-upper lobectomy [78]. Communication with the surgical team regarding the presence of a bronchial blocker in the surgical side is crucial. Another potential and dangerous complication with the bronchial cuff of the Univent has been reported: the cuff of the bronchial blocker was inflated mistakenly near the tracheal lumen, precluding all airflow and producing respiratory arrest [79].

Complications with the Arndt® blocker include a report of a sheared balloon of the Arndt® blocker that occurred when the blocker was removed through the multiport blocker side [80]. It is advised that when an independent bronchial blocker is not in use it needs to be removed with the multiport connector in place rather than through the connector to prevent shredded material into the single-lumen endotracheal tube. Another near-fatal complication reported with the use of the Arndt® blocker occurred when the fully inflated balloon of the blocker dislodged into the patient's trachea, leading to a complete airway obstruction. Severe air trapping led to pulseless activity in the patient, who was undergoing a rupture descending thoracic aortic aneurysm. A prompt deflation of the bronchial blocker cuff resolved the problem [81].

Another complication reported with the Arndt® blocker involved inadvertent resection of the guide wire and part of the tip of the bronchial blocker during stapler resection of the left lower lobe; this complication required surgical reexploration after unsuccessful removal of the bronchial blocker after extubation [72].

There are not yet any reports of complications with the Cohen® blocker or the Fuji Uniblocker®, perhaps because of their relatively recent introduction and use. With the use of the current bronchial blockers, there have not yet been any

reports of a ruptured trachea or bronchus; however, the number of complications with the DLTs is higher than for bronchial blockers.

Lung Isolation in Patients with Tracheostomy in Place

OLV can be a challenge in patients with a tracheostomy in place because the airway has been shortened and the stoma can be small and restrictive. Although a shortened version of a DLT for tracheostomy patients has been used [82, 83], there is no shortened DLT available for tracheostomy patients in the United States. An alternative to achieve successful lung separation through a tracheostomized patient involves the use of a bronchial blocker, either attached to a single-lumen endotracheal tube such as the Univent® blocker [84, 85], or passed independently through a Shiley 8.0-mm ID tracheostomy tube (Mallinckrodt, St. Louis MO) with the Arndt® bronchial blocker [68], or placed independently through a single-lumen endotracheal tube [86]. An alternative way to manage these cases is with the Cohen® Blocker [7] or the Fuji Uniblocker® [8]; when passing a 9 F bronchial blocker through a tracheostomy tube, the recommended flexible fiberoptic bronchoscope should be 3.5-mm ID so the independent blocker and the fiberscope can navigate together to achieve optimal position of these devices into the designed bronchus. In some instances when using a Shiley tracheostomy tube, the multiport connector is attached to the ventilating port of the Shiley cannula to maintain the bronchial blocker in place. Optimal position is achieved with the fiberoptic bronchoscope. Figure 16.14 displays the use of an independent blocker through a tracheostomy stoma.

Lung Collapse During Lung Isolation

A challenge for every anesthesiologist is to properly position a lung isolation device and make it work by allowing the lung to collapse. In a study [5] comparing the Broncho-Cath left-sided DLT with the Univent® torque control blocker and the Arndt® wire-guided blocker, it was shown that the average time for lung collapse is 17 min for a DLT (spontaneous lung collapse without suction) versus 19–26 min for the Univent® or Arndt® bronchial blocker (assisted with suction). Once lung isolation was achieved, however, the overall clinical performance was similar for the three devices studied.

Another study [8] involving left-sided DLTs and comparing it with the Arndt®, the Cohen®, or the Fuji® blocker showed that the surgical exposure was equivalent among the devices studied. However, the bronchial blockers required longer time to position and were more prone to intraoperative reposition. It is important to emphasize that these two studies involved at least one senior thoracic anesthesiologist with broad experience with lung isolation devices.

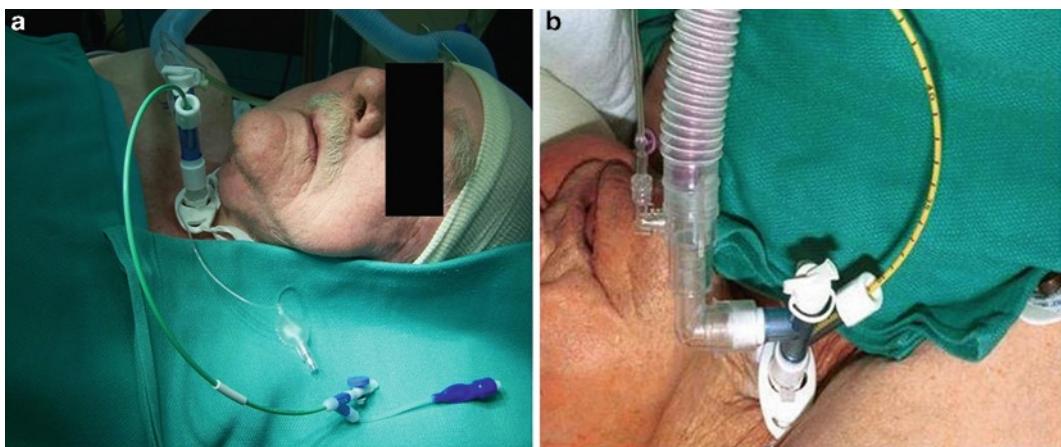


FIG. 16.14. (a) Cohen® blocker in a patient with a tracheostomy. (b) Use of an Arndt® blocker via a tracheostomy.

TABLE 16.6. Advantages and disadvantages of DLTs and bronchial blockers.

Double-lumen endotracheal tubes	Bronchial blockers (Arndt®, Cohen®, Fuji®)
<p><i>Advantages</i></p> <ul style="list-style-type: none"> • Large lumen facilitates suctioning • Best device for absolute indications for lung separation, to protect the lung from soiling • Conversion from 2- to 1-lung ventilation and back easy and reliable <p><i>Disadvantages</i></p> <ul style="list-style-type: none"> • Difficulties in selecting proper size • More difficult to place during laryngoscopy • Potential damage to tracheal cuff during intubation • Rare major tracheobronchial injuries 	<ul style="list-style-type: none"> • Easy recognition of anatomy if the tip of a single tube is above carina • Best device for patients with difficult airways • Cuff damage during intubation rare • No need to replace a tube if mechanical ventilation is needed • Small channel for suctioning • Conversion from 1- to 2- then to 1-lung ventilation problematic more complicated • High maintenance device (frequent dislodgement or loss of seal during surgery)
Modified from Campos [55]	

A recent study [87] has shown that denitrogenation of the lung which is to be collapsed with a FiO_2 1.0 is a useful strategy to improve surgical conditions during OLV; in contrast, the use of air in the inspired gas mixture during two-lung ventilation and prior to OLV delays lung collapse during OLV. Table 16.6 displays the advantages and disadvantages of DLTs and bronchial blockers.

Future Trends in Lung Isolation

With the advances in thoracic, cardiac, esophageal surgery, and minimally invasive surgery, it has led to an increased need for lung isolation techniques among anesthesiologists. A previous study [35] has shown that anesthesiologists with limited thoracic experience often fail to correctly place lung isolation devices. Increased clinical experience would likely reduce this failure rate, but greater experience may not be possible, particularly for anesthesiologists working in centers that perform

relatively few thoracic cases. Therefore, improved nonclinical training methods are needed.

Anesthesia simulators have been used to enhance learning and to improve performance [88–90], usually under the personal direction of an experienced clinician. Therefore, one educational approach to lung isolation techniques might involve training on an airway simulator mentored by an experienced thoracic anesthesiologist. An alternative is to train in a fiberoptic bronchoscopy simulator [91] on lung isolation techniques particularly for the occasional anesthesiologist who does not perform thoracic cases on a regular basis. It is the author's personal opinion that every surgical center that performs lung isolation techniques must consider the development of a pulmonary workstation along with simulator training facility to enhance teaching to residents, fellows, and staff anesthesiologists. Figure 16.15 displays a pulmonary workstation including simulator. Also, a free online bronchoscopy simulator is available on the website www.thoracicanesthesia.com to teach anesthesiologists tracheobronchial anatomy (see Fig. 16.16).

FIG. 16.15. Ideal teaching facility with a pulmonary work station for placement of lung isolation devices by trainees.

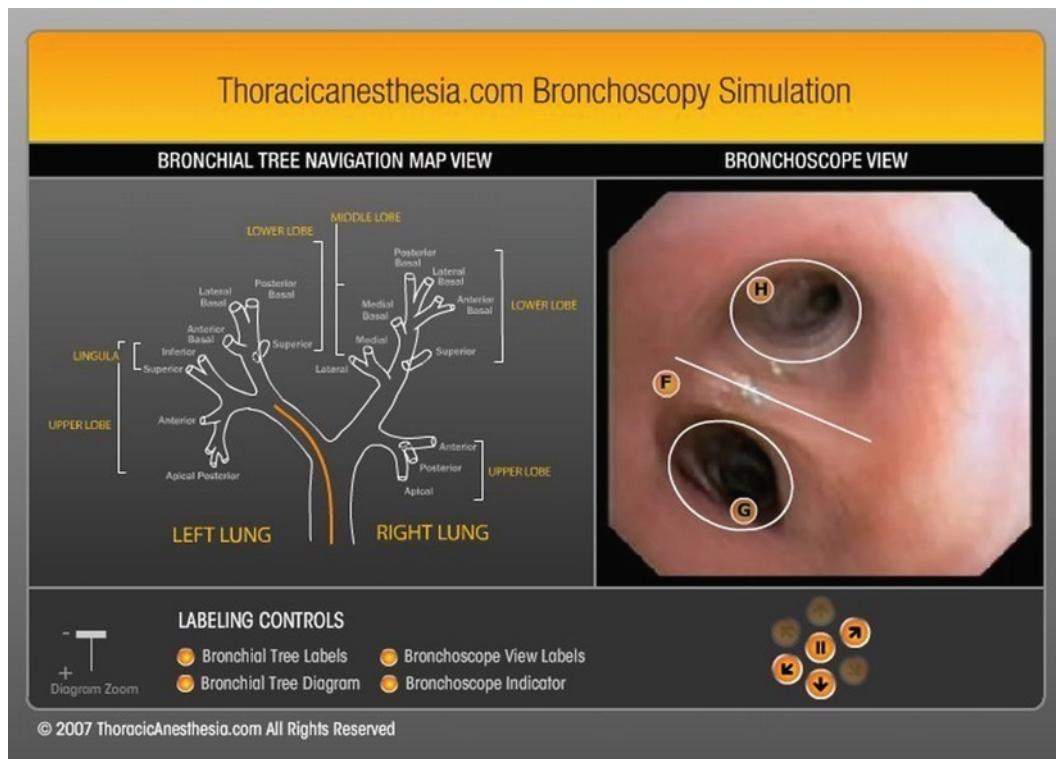
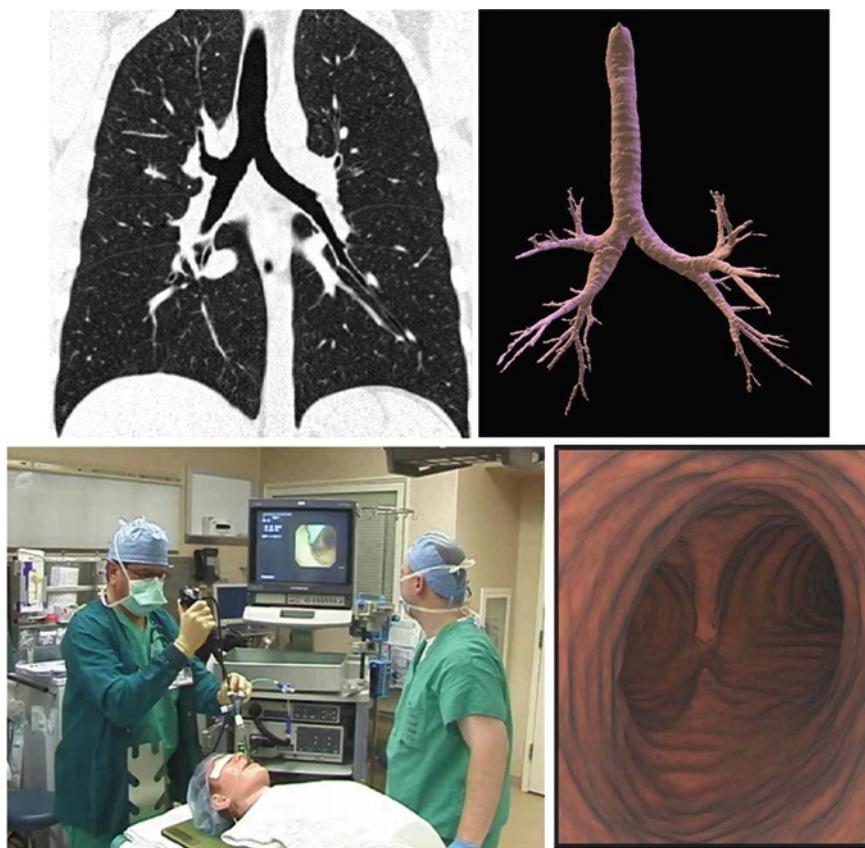


FIG. 16.16. The free online bronchoscopy simulator at www.thoracicanesthesia.com. The user can navigate the tracheobronchial tree using real-time video by clicking on the lighted directional arrows under the “Bronchoscopic view” (right). Clicking on the labels on the “Bronchoscopic view” gives details of the anatomy seen. The process is aided by the “Bronchial Tree Navigational Map” (left), which shows the simultaneous location of the bronchoscope as the orange line in the airway.

Summary

The basic principle of successful lung separation requires (1) recognition of tracheobronchial anatomy with a posterior-anterior chest radiograph in the preoperative evaluation and with flexible fiberoptic bronchoscopy in the perioperative period, (2) familiarity and skills with flexible fiberoptic bronchoscopy, and (3) familiarity and expertise with DLTs and bronchial blockers.

Because of its greater margin of safety, a left-sided DLT is the more common and easiest device used during lung separation. A right-sided DLT is recommended for a left-sided pneumonectomy or any contraindication to placement of a left-sided DLT. For patients with a difficult abnormal airway or a tracheostomy in place, the use of a bronchial blocker is indicated. Bronchial blockers require more time for placement and are more prone to intraoperative dislodgement. Lung collapse is facilitated with a denitrogenation technique using FiO_2 1.0 during two-lung ventilation prior to lung collapse. Every lung isolation device placement requires auscultation and clamping maneuvers followed by a fiberoptic bronchoscopy to obtain 100% success during lung separation techniques. The optimal position of these devices (DLTs and bronchial blockers) is achieved best with the use of fiberoptic bronchoscopy techniques with the patient first in the supine and then in the lateral decubitus position or whenever repositioning of the device is needed.

Clinical Case Discussion

Case: A 60-year-old female, weight 61 kg and is 161 cm tall, has a left lower lobe mass and is scheduled for a left lower lobectomy (Fig. 16.17a, b). She is a former smoker

and the predicted value of forced expiratory volume in 1 s (FEV₁) is 75% of the predicted value. She has no significant known comorbidities and past history otherwise unremarkable.

Questions

- What lung isolation device will be indicated?
- What side and size of lung isolation device will be indicated?
- What anatomical structures in the chest radiograph are relevant while planning the use of lung isolation devices?
- What are the different alternatives for lung isolation devices?
- What technique should be used to achieve optimal position of lung isolation devices?
- What are the common problems in the intraoperative period with lung isolation devices?
- What are the complications associated with lung isolation devices?

Focus on the Patient's Gender, Size, Height, and Preoperative Chest Radiograph

- To determine the lung isolation device.
- Focus on the use of left-sided DLT for routine, uncomplicated cases or a right-sided DLT for selective cases.
- Focus on the indication of lung isolation.
- Knowledge of tracheobronchial anatomy and the use of flexible fiberoptic bronchoscopy to confirm device placement are essential for success on lung isolation.
- Alternative devices for lung isolation such as bronchial blockers should be considered in specific cases.

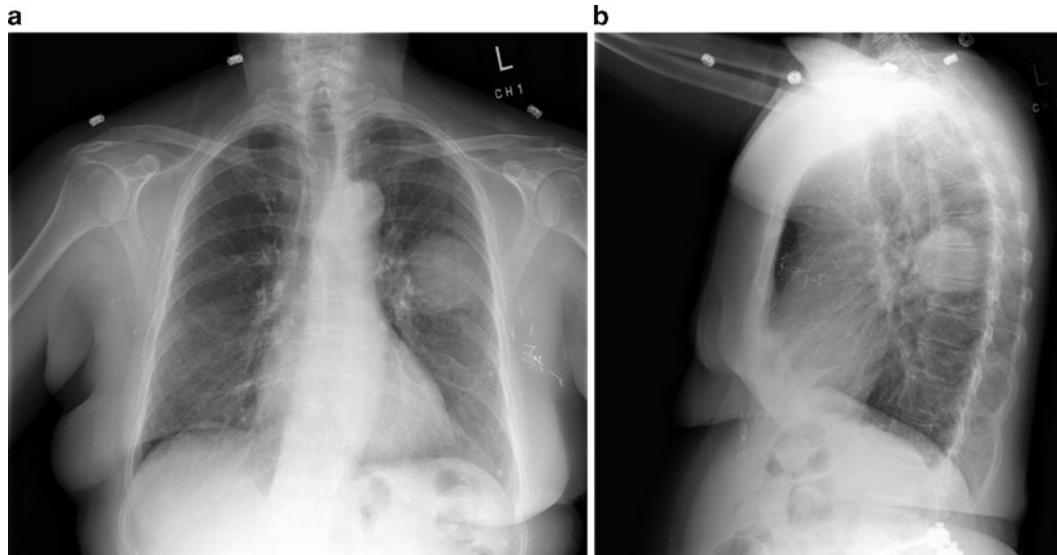


FIG. 16.17. (a, b) Chest X-ray of a female patient with a carcinoma of the left lower lobe undergoing lobectomy.

Choice of Lung Isolation Device

- If there is nothing in the patient's history or physical examination to suggest the possibility of difficult airway in a left- or right-sided DLT, depending on the clinician's preference, would be equivalent first choices to manage this case.
- The patient's sex and height suggest that either a 35 F or 37 F DLT would be appropriate, the choice can be further refined by measuring the tracheal width on the PA chest X-ray (see Fig. 16.1).
- In the absence of a difficult airway, the problem of intraoperative displacement with bronchial blockers makes them a second choice for lung isolation in this patient.
- Correct positioning of the device for lung isolation should be confirmed with fiberoptic bronchoscopy.

Expected Intraoperative Problems During Lung Isolation

- Malpositions and the potential for tracheobronchial injuries.

References

1. Campos JH. Current techniques for perioperative lung isolation in adults. *Anesthesiology*. 2002;97:1295–301.
2. Campos JH. Progress in lung separation. *Thorac Surg Clin*. 2005;15:71–83.
3. Lewis Jr JW, Serwin JP, Gabriel FS, Bastanfar M, Jacobsen G. The utility of a double-lumen tube for one-lung ventilation in a variety of noncardiac thoracic surgical procedures. *J Cardiothorac Vasc Anesth*. 1992;6:705–10.
4. Campos JH. An update on bronchial blockers during lung separation techniques in adults. *Anesth Analg*. 2003;97:1266–74.
5. Campos JH, Kernstine KH. A comparison of a left-sided Broncho-Cath with the torque control blocker univent and the wire-guided blocker. *Anesth Analg*. 2003;96:283–9.
6. Arndt GA, Kranner PW, Rusy DA, Love R. Single-lung ventilation in a critically ill patient using a fiberoptically directed wire-guided endobronchial blocker. *Anesthesiology*. 1999;90:1484–6.
7. Cohen E. The Cohen flexitip endobronchial blocker: an alternative to a double lumen tube. *Anesth Analg*. 2005;101:1877–9.
8. Narayanaswamy M, McRae K, Slinger P, et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. *Anesth Analg*. 2009;108:1097–101.
9. Bjork VO, Carlens E. The prevention of spread during pulmonary resection by the use of a double-lumen catheter. *J Thorac Surg*. 1950;20:151–7.
10. Campos JH, Massa FC, Kernstine KH. The incidence of right upper-lobe collapse when comparing a right-sided double-lumen tube versus a modified left double-lumen tube for left-sided thoracic surgery. *Anesth Analg*. 2000;90:535–40.
11. Seymour AH, Prakash N. A cadaver study to measure the adult glottis and subglottis: defining a problem associated with the use of double-lumen tubes. *J Cardiothorac Vasc Anesth*. 2002;16:196–8.
12. Sivalingam P, Tio R. Tension pneumothorax, pneumomediastinum, pneumoperitoneum, and subcutaneous emphysema in a 15-year-old Chinese girl after a double-lumen tube intubation and one-lung ventilation. *J Cardiothorac Vasc Anesth*. 1999;13:312–5.
13. Bardoczky G, d'Hollander A, Yernault JC, et al. On-line expiratory flow-volume curves during thoracic surgery: occurrence of auto-PEEP. *Br J Anaesth*. 1994;72:25–8.
14. Sakuragi T, Kumano K, Yasumoto M, Dan K. Rupture of the left main-stem bronchus by the tracheal portion of a double-lumen endobronchial tube. *Acta Anaesthesiol Scand*. 1997;41:1218–20.
15. Hannallah M, Gomes M. Bronchial rupture associated with the use of a double-lumen tube in a small adult. *Anesthesiology*. 1989;71:457–8.
16. Brodsky JB, Macario A, Mark JB. Tracheal diameter predicts double-lumen tube size: a method for selecting left double-lumen tubes. *Anesth Analg*. 1996;82:861–4.
17. Chow MY, Liam BL, Lew TW, Chelliah RY, Ong BC. Predicting the size of a double-lumen endobronchial tube based on tracheal diameter. *Anesth Analg*. 1998;87:158–60.
18. Amar D, Desiderio DP, Heerd PM, et al. Practice patterns in choice of left double-lumen tube size for thoracic surgery. *Anesth Analg*. 2008;106:379–83.
19. Eberle B, Weiler N, Vogel N, Kauczor HU, Heinrichs W. Computed tomography-based tracheobronchial image reconstruction allows selection of the individually appropriate double-lumen tube size. *J Cardiothorac Vasc Anesth*. 1999;13:532–7.
20. Brodsky JB, Benumof JL, Ehrenwerth J, Ozaki GT. Depth of placement of left double-lumen endobronchial tubes. *Anesth Analg*. 1991;73:570–2.
21. Boucek CD, Landreneau R, Freeman JA, Strollo D, Bircher NG. A comparison of techniques for placement of double-lumen endobronchial tubes. *J Clin Anesth*. 1998;10:557–60.
22. Brodsky JB, Lemmens HJ. Left double-lumen tubes: clinical experience with 1,170 patients. *J Cardiothorac Vasc Anesth*. 2003;17:289–98.
23. Benumof JL, Partridge BL, Salvatierra C, Keating J. Margin of safety in positioning modern double-lumen endotracheal tubes. *Anesthesiology*. 1987;67:729–38.
24. McKenna MJ, Wilson RS, Botelho RJ. Right upper lobe obstruction with right-sided double-lumen endobronchial tubes: a comparison of two tube types. *J Cardiothorac Anesth*. 1988;2:734–40.
25. Campos JH, Gomez MN. Pro: right-sided double-lumen endotracheal tubes should be routinely used in thoracic surgery. *J Cardiothorac Vasc Anesth*. 2002;16:246–8.
26. Bussières JS, Lacasse Y, Côté D, et al. Modified right-sided Broncho-Cath® double lumen tube improves endobronchial positioning: a randomized study. *Can J Anaesth*. 2007;54:276–82.
27. Stene R, Rose M, Weinger MB, Benumof JL, Harrell J. Bronchial trifurcation at the carina complicating use of a double-lumen tracheal tube. *Anesthesiology*. 1994;80:1162–3.
28. Ehrenfeld JM, Walsh JL, Sandberg WS. Right- and left-sided Mallinckrodt double-lumen tubes have identical clinical performance. *Anesth Analg*. 2008;106:1847–52.
29. Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic anesthesia. *Curr Opin Anaesthesiol*. 2009;22:4–10.
30. Klein U, Karzai W, Bloos F, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes

- for thoracic anaesthesia: a prospective study. *Anesthesiology*. 1998;88:346–50.
31. Sherry K. Management of patients undergoing oesophagectomy. In: Gray AJG, Hoile RW, Ingram GS, Sherry K, editors. *The Report of the National Confidential Enquiry into Perioperative Deaths 1996/1997. NCEPOD*: London; 1998. p. 57–61.
 32. Pennefather SH, Russell GN. Placement of double lumen tubes – time to shed light on an old problem. *Br J Anaesth*. 2000;84: 308–10.
 33. Seymour AH, Prasad B, McKenzie RJ. Audit of double-lumen endobronchial intubation. *Br J Anaesth*. 2004;93:525–7.
 34. Slinger P. A view of and through double-lumen tubes. *J Cardiothorac Vasc Anesth*. 2003;17:287–8.
 35. Campos JH, Hallam EA, Van Natta T, Kernstine KH. Devices for lung isolation used by anesthesiologists with limited thoracic experience: comparison of double-lumen endotracheal tube, Univent torque control blocker, and Arndt wire-guided endobronchial blocker. *Anesthesiology*. 2006;104:261–6.
 36. Lohser J, Brodsky JB. Silbronco double-lumen tube. *J Cardiothorac Vasc Anesth*. 2006;20:129–31.
 37. Hagihi S, Takashina M, Mashimo T. Application of a newly designed right-sided, double-lumen endobronchial tube in patients with a very short right mainstem bronchus. *Anesthesiology*. 2008;109:565–8.
 38. Ghosh S, Falter F, Goldsmith K, Arrowsmith JE. The Papworth BiVent tube: a new device for lung isolation. *Anaesthesia*. 2008;63:996–1000.
 39. Ghosh S, Klein AA, Prabhu M, Falter F, et al. The Papworth BiVent tube: a feasibility study of a novel double-lumen endotracheal tube and bronchial blocker in human cadavers. *Br J Anaesth*. 2008;101:424–8.
 40. Saito S, Dohi S, Naito H. Alteration of double-lumen endobronchial tube position by flexion and extension of the neck. *Anesthesiology*. 1985;62:696–7.
 41. Yüceyar L, Kaynak K, Cantürk E, Aykaç B. Bronchial rupture with a left-sided polyvinylchloride double-lumen tube. *Acta Anaesthesiol Scand*. 2003;47:622–5.
 42. Liu H, Jahr JS, Sullivan E, Waters PF. Tracheobronchial rupture after double-lumen endotracheal intubation. *J Cardiothorac Vasc Anesth*. 2004;18:228–33.
 43. Benumof JL, Wu D. Tracheal tear caused by extubation of a double-lumen tube. *Anesthesiology*. 2002;97:1007–8.
 44. Sucato DJ, Gergis M. Bilateral pneumothoraces, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, and subcutaneous emphysema following intubation with a double-lumen endotracheal tube for thoracoscopic anterior spinal release and fusion in a patient with idiopathic scoliosis. *J Spinal Disord Tech*. 2002;15:133–8.
 45. Weng W, DeCrosta DJ, Zhang H. Tension pneumothorax during one-lung ventilation: a case report. *J Clin Anesth*. 2002;14: 529–31.
 46. Fitzmaurice BG, Brodsky JB. Airway rupture from double-lumen tubes. *J Cardiothorac Vasc Anesth*. 1999;13:322–9.
 47. Knoll H, Ziegeler S, Schreiber JU, et al. Airway injuries after one-lung ventilation: a comparison between double-lumen tube and endobronchial blocker: a randomized, prospective, controlled trial. *Anesthesiology*. 2006;105:471–7.
 48. Campos JH. Effects of oxygenation during selective lobar versus total lung collapse with or without continuous positive airway pressure. *Anesth Analg*. 1997;85:583–6.
 49. Campos JH, Ledet C, Moyers JR. Improvement of arterial oxygen saturation with selective lobar bronchial block during hemorrhage in a patient with previous contralateral lobectomy. *Anesth Analg*. 1995;81:1095–6.
 50. Amar D, Desiderio DP, Bains MS, Wilson RS. A novel method of one-lung isolation using a double endobronchial blocker technique. *Anesthesiology*. 2001;95:1528–30.
 51. Espí C, García-Guasch R, Ibáñez C, Fernández E, Astudillo J. Selective lobar blockade using an Arndt endobronchial blocker in 2 patients with respiratory compromise who underwent lung resection. *Arch Bronconeumol*. 2007;43:346–8.
 52. Ng JM, Hartigan PM. Selective lobar bronchial blockade following contralateral pneumonectomy. *Anesthesiology*. 2003;98: 268–70.
 53. Hagihi S, Maki N, Kawaguchi M, Slinger P. Selective bronchial blockade in patients with previous contralateral lung surgery. *J Cardiothorac Vasc Anesth*. 2002;16:638–42.
 54. Campos JH. Update on selective lobar blockade during pulmonary resections. *Curr Opin Anaesthesiol*. 2009;22:18–22.
 55. Campos JH. Which device should be considered the best for lung isolation: double-lumen endotracheal tube versus bronchial blockers. *Curr Opin Anaesthesiol*. 2007;20:27–31.
 56. Hagihi S, Takashina M, Mori T, Yoshiya I. One-lung ventilation in patients with difficult airways. *J Cardiothorac Vasc Anesth*. 1998;12:186–8.
 57. Baraka A. The univent tube can facilitate difficult intubation in a patient undergoing thoracoscopy. *J Cardiothorac Vasc Anesth*. 1996;10:693–4.
 58. Ransom ES, Carter SL, Mund GD. Univent tube: a useful device in patients with difficult airways. *J Cardiothorac Vasc Anesth*. 1995;9:725–7.
 59. Campos JH. Difficult airway and one-lung ventilation. *Curr Rev Clin Anesth*. 2002;22:197–208.
 60. García-Aguado R, Mateo EM, Tommasi-Rosso M, et al. Thoracic surgery and difficult intubation: another application of univent tube for one-lung ventilation. *J Cardiothorac Vasc Anesth*. 1997;11:925–6.
 61. García-Aguado R, Mateo EM, Onrubia VJ, Bolinches R. Use of the Univent System tube for difficult intubation and for achieving one-lung anaesthesia. *Acta Anaesthesiol Scand*. 1996;40:765–7.
 62. Takenaka I, Aoyama K, Kadoya T. Use of the univent bronchial-blocker tube for unanticipated difficult endotracheal intubation. *Anesthesiology*. 2000;93:590–1.
 63. Campos JH. How to achieve successful lung separation. *SAJAA*. 2008;14:22–6.
 64. Arndt GA, DeLessio ST, Kranner PW, et al. One-lung ventilation when intubation is difficult—presentation of a new endobronchial blocker. *Acta Anaesthesiol Scand*. 1999;43:356–8.
 65. Arndt GA, Buchika S, Kranner PW, DeLessio ST. Wire-guided endobronchial blockade in a patient with a limited mouth opening. *Can J Anaesth*. 1999;46:87–9.
 66. Grocott HP, Scales G, Schindlerle D, King K. A new technique for lung isolation in acute thoracic trauma. *J Trauma*. 2000;49: 940–2.
 67. Byhahn C, Habler OP, Bingold TM, et al. The wire-guided endobronchial blocker: applications in trauma patients beyond mere single-lung ventilation. *J Trauma*. 2006;61:755–9.
 68. Campos JH, Kernstine KH. Use of the wire-guided endobronchial blocker for one-lung anaesthesia in patients with airway abnormalities. *J Cardiothorac Vasc Anesth*. 2003;17:352–4.

69. Kabon B, Waltl B, Leitgeb J, Kapral S, Zimpfer M. First experience with fiberoptically directed wire-guided endobronchial blockade in severe pulmonary bleeding in an emergency setting. *Chest*. 2001;120:1399–402.
70. Kazari W. Alternative method to deflate the operated lung when using wire-guided endobronchial blockade. *Anesthesiology*. 2003;99:239–40.
71. Campos JH. In response: an Alternative method to deflate the operated lung when using wire guided endobronchial blockade. *Anesthesiology*. 2003;99:241.
72. Soto RG, Oleszak SP. Resection of the Arndt bronchial blocker during stapler resection of the left lower lobe. *J Cardiothorac Vasc Anesth*. 2006;20:131–2.
73. Roscoe A, Kanellakos GW, McRae K, Slinger P. Pressures exerted by endobronchial devices. *Anesth Analg*. 2007;104:655–8.
74. Lizuka T, Tanno M, Hamada Y, Shiga T, Ohe Y. Uniblocker® bronchial blocker tube to facilitate one-lung ventilation during thoracoscopic surgery. *Anesthesiology*. 2007;108:A1815.
75. Campos JH, Kernstine KH. A structural complication in the torque control blocker Univent: fracture of the blocker cap connector. *Anesth Analg*. 2003;96:630–1.
76. Peragallo RA, Swenson JD. Congenital tracheal bronchus: the inability to isolate the right lung with a univent bronchial blocker tube. *Anesth Analg*. 2000;91:300–1.
77. Asai T. Failure of the Univent bronchial blocker in sealing the bronchus. *Anaesthesia*. 1999;54:97.
78. Thielmeier KA, Anwar M. Complication of the Univent tube. *Anesthesiology*. 1996;84:491.
79. Dougherty P, Hannallah M. A potentially serious complication that resulted from improper use of the Univent tube. *Anesthesiology*. 1992;77:835.
80. Prabhu MR, Smith JH. Use of the Arndt wire-guided endobronchial blocker. *Anesthesiology*. 2002;97:1325.
81. Sandberg WS. Endobronchial blocker dislodgement leading to pulseless electrical activity. *Anesth Analg*. 2005;100:1728–30.
82. Brodsky JB, Tobler HG, Mark JB. A double-lumen endobronchial tube for tracheostomies. *Anesthesiology*. 1991;74:387–8.
83. Saito T, Naruke T, Carney E, et al. New double intrabronchial tube (Naruke tube) for tracheostomized patients. *Anesthesiology*. 1998;89:1038–9.
84. Bellver J, García-Aguado R, De Andrés J, Valía JC, Bolinches R. Selective bronchial intubation with the univent system in patients with a tracheostomy. *Anesthesiology*. 1993;79:1453–4.
85. Dhamee MS. One-lung ventilation in a patient with a fresh tracheostomy using the tracheostomy tube and a Univent endobronchial blocker. *J Cardiothorac Vasc Anesth*. 1997;11:124–5.
86. Tobias JD. Variations on one-lung ventilation. *J Clin Anesth*. 2001;13:35–9.
87. Ko R, McRae K, Darling G, et al. The use of air in the inspired gas mixture during two-lung ventilation delays lung collapse during one-lung ventilation. *Anesth Analg*. 2009;108:1092–6.
88. Hesselfeldt R, Kristensen MS, Rasmussen LS, et al. Evaluation of the airway of the SimMan® full-scale patient simulator. *Acta Anaesthesiol Scand*. 2005;49:1339–45.
89. Wong AK. Full scale computer simulators in anesthesia training and evaluation. *Can J Anaesth*. 2004;51:455–64.
90. Nyssen AS, Larbuisson R, Janssens M, et al. A comparison of the training value of two types of anesthesia simulators: computer screen-based and mannequin-based simulators. *Anesth Analg*. 2002;94:1560–5.
91. Duffy CH, Myles PS. Review: thoracic-anesthesia.com. *J Cardiothorac Vasc Anesth*. 2008;22:644.

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Key Points

- Recognition of a difficult airway prior to the use of lung isolation devices is essential.
- Radiological studies must be reviewed, including a posterior–anterior chest radiograph and computer tomography scan of the chest.
- Securing the airway first is a must in patients with difficult airways requiring lung isolation.
- The use of an independent bronchial blocker is the first-line choice in patients who require nasotracheal intubation.
- The use of the airway exchange catheter is recommended during placement of double-lumen endotracheal tubes in patients with difficult airways.

Introduction

One-lung ventilation (OLV) in the thoracic surgical patient can be achieved with the use of a double-lumen endotracheal tube (DLT) or an independent bronchial blocker [1]. A number of patients requiring lung isolation have a potentially difficult airway because of previous radiation to the neck or previous surgery to the tongue and larynx [2]. In order to manage these patients with difficult airways, it is important to understand the normal anatomy of the tracheobronchial tree as well as of the anatomical distances of the airway [3].

Normal Anatomy of the Airway and Tracheobronchial Tree

The trachea is a cartilaginous and fibromuscular tubular structure that extends from the inferior aspect of the cricoid cartilage to the level of the carina [4]. The adult trachea is an average 15 cm long. The trachea is composed of 16–22 C-shaped cartilages. The cartilages compose the anterior and lateral walls of the trachea and are connected posteriorly by the membranous wall of the trachea, which lacks cartilage and is supported by the trachealis muscle. The average diameter in a normal trachea is 22 mm in men and 19 mm in women. In men, the coronal diameter ranges from 13 to 22 mm and the sagittal diameter ranges from 13 to 27 mm. In women, the average coronal diameter is 10–21 mm and the sagittal is 10–23 mm [4, 5]. The tracheal wall is about 3 mm in thickness in both men and women, with a tracheal lumen that is often ovoid in shape.

The trachea is located in the midline position, but often can be deviated to the right at the level of the aortic arch, with a greater degree of displacement in the setting of an atherosclerotic aorta, advanced age, or in the presence of severe chronic obstructive pulmonary disease (COPD). With COPD or aging, the lateral diameter of the trachea may decrease, with an increase in the anteroposterior diameter. Conversely, COPD may also lead to softening of the tracheal rings, with

a decrease in the anteroposterior diameter of the trachea [6]. The cricoid cartilage is the narrowest part of the trachea with an average diameter of 17 mm in men and 13 mm in women.

The trachea bifurcates at the carina into the right and left mainstem bronchus. An important fact is that the tracheal lumen narrows slightly as it progresses towards the carina. The tracheal bifurcation is located at the level of the sternal angle anteriorly and the 5th thoracic vertebra posteriorly. The right mainstem bronchus lies in a more vertical orientation related to the trachea, whereas the left mainstem bronchus lies in a more horizontal plane. The right mainstem bronchus continues as the bronchus intermedius after the takeoff of the right upper lobe bronchus. In men, the distance from the tracheal carina to the takeoff of the right upper lobe bronchus is an average of 2.0 cm, whereas it is approximately 1.5 cm in women. Also it is known that one in every 250 individuals from the general population may have an abnormal takeoff of the right upper lobe bronchus emerging from above the tracheal carina on the right side [7]. The diameter of the right mainstem bronchus is an average of 17.5 mm in men and 14 mm in women. The trifurcation of the right upper lobe bronchus consists of the apical, anterior, and posterior division. This is an important landmark to identify while performing fiberoptic bronchoscopy in order to distinguish the right from the left mainstem bronchus. The distance from the tracheal carina to the bifurcation of the left upper and lower lobes is approximately 5.0 cm in men and 4.5 cm in women and is longer than the right mainstem bronchus (1.5–2 cm). The left upper lobe bronchus has a superior and inferior division. Figure 17.1 displays the anatomical distances of the airway.

Patients requiring OLV may be identified during the preoperative evaluation to have a potentially difficult airway. Others present with airways that are unexpectedly difficult to intubate after induction of anesthesia. It is estimated that between 5 and 8% of patients with primary lung carcinoma also have a carcinoma of the pharynx, usually in the epiglottic area [2]. Many of these patients have had previous radiation therapy on the neck or previous airway surgery, such as hemimandibulectomy or hemiglossectomy, making intubation and achievement of OLV difficult due to distorted upper airway anatomy. Also, a patient who requires OLV might have distorted anatomy at or beyond the tracheal carina, such as a descending thoracic aortic aneurysm compressing the entrance of the left mainstem bronchus or an intraluminal or extraluminal tumor near the tracheobronchial bifurcation that makes the insertion of a left-sided DLT relatively difficult or impossible.

Preoperative Evaluation of the Difficult Airway and Lung Isolation Techniques

According to the ASA practice guideline for management of the difficult airway [8], an airway is termed difficult when conventional laryngoscopy reveals a grade III view (just the epiglottis is seen) or a grade IV view (just part of the soft

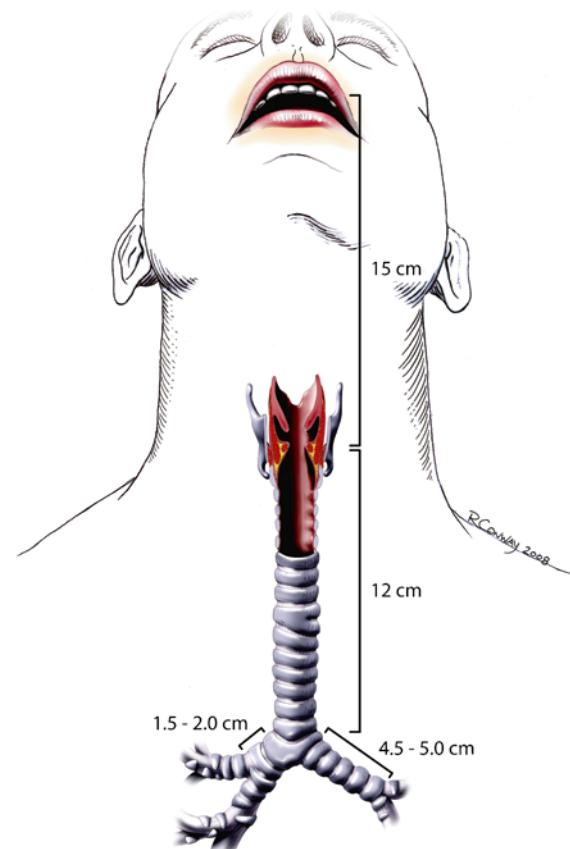


FIG. 17.1. The anatomical distances of the airway. The average length from the incisors to the vocal cords is approximately 15 cm, and the distance from the vocal cords to the tracheal carina is 12 cm. The average distance from the tracheal carina to the takeoff of the right-upper bronchus is 2.0 cm in men and 1.5 cm in women. The distance from the tracheal carina to the takeoff of the left upper and left lower lobe is approximately 5.0 cm in men and 4.5 cm in women. These anatomical distances apply to individuals with a height of 170 cm [3].

palate is seen). Once the airway is recognized as being potentially difficult, a careful examination of the patient ensues. Previous anesthesia records should be examined for a history of airway management. Patients should be asked to open their mouths as widely as possible and extend their tongues. The mandibular opening should be assessed and the pharyngeal anatomy observed. The length of the submental space should also be noted. Patients should be evaluated from side to side to assess any degree of maxillary overbite and their ability to assume the sniffing position. Also, the patency of the nostrils must be assessed in patients who cannot open their mouths, as a nasotracheal approach might be considered. In patients who had received radiation therapy to the neck, a palpation of the external surface of the neck is necessary to determine if this presents very hard, rigid-consistency tissue. Also, the neck range motion should be checked to determine the flexion and extension prior to laryngoscopy. For patients who have a

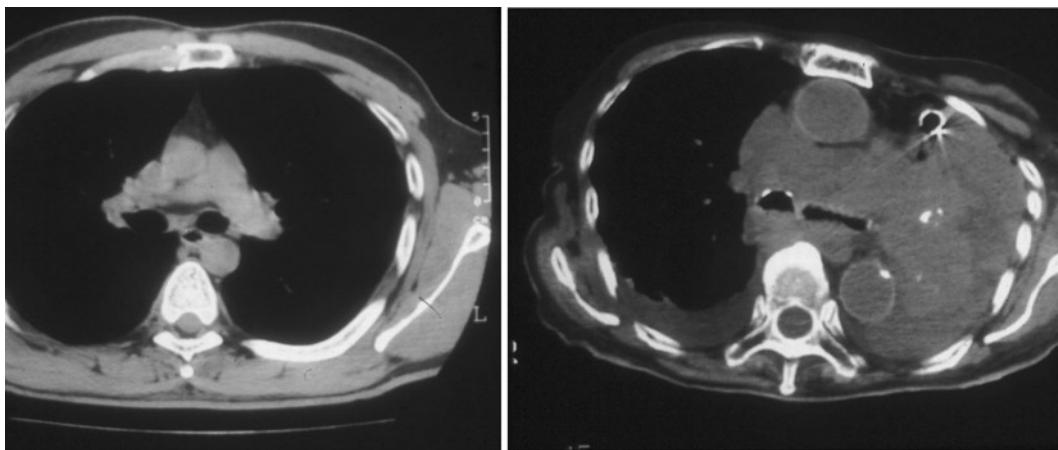


FIG. 17.2. Computed tomography (CT) scans from just below the level of the carinal bifurcation. *Left:* CT from a patient with no compression of the airway. *Right:* CT from patient scheduled for left lung biopsy. The patient has a left-sided lung tumor and effusion, which compresses the left mainstem bronchus. This bronchial compression was not evident on the chest X-ray. It may be difficult to place a left-sided double-lumen endobronchial tube (DLT) in this patient. A right-sided DLT or a bronchial blocker would be the preferred method of lung isolation for this patient under fiberoptic bronchoscopy guidance.

tracheostomy cannula in place, the inlet of the stoma and the circumferential diameter must be assessed when considering replacing the tracheostomy cannula with a specific device to achieve OLV.

Another group of patients considered to have difficult airways during OLV are those who have distorted anatomy at the entrance of the mainstem bronchus. Such anomalies can be found by reviewing the chest radiographs and by reviewing the computer tomography scans of the chest regarding the mainstem bronchus diameter and anatomy, which can be distorted or compressed (see Fig. 17.2). Also, in some specific patients an examination with a flexible fiberoptic bronchoscope under local anesthesia and sedation will be necessary to assess a distorted area of the airway prior to the selection of a specific device to achieve OLV. Table 17.1 displays the patients at risk of having a difficult intubation during OLV [9].

TABLE 17.1. Characteristics of patients at risk of having a difficult intubation during one-lung ventilation.

Upper airway	Lower airway
Short neck and increased neck circumference	Existing tracheostomy in place
Prominent upper incisors with a receding mandible	Distorted anatomy (trachea/bronchus)
Limited cervical mobility	Compression at the entrance of left mainstem bronchus by a tumor or a descending thoracic aortic aneurysm
Limited jaw opening due to previous surgery	
Radiation therapy of the neck	
Hemiglossectomy/ hemimandibulectomy	
Tumors (mouth, tongue, epiglottis)	

bronchoscope, a single-lumen endotracheal tube can be passed through the laryngeal mask airway [13].

Difficult Airway and Lung Isolation: Securing the Airway First

In patients who require OLV and present with the dilemma of a difficult airway, the primary goal after appropriate airway anesthesia is achieved is to establish an airway with a single-lumen endotracheal tube placed orally with the aid of a flexible fiberoptic bronchoscope. In selected patients who seem easy to ventilate, this may be performed after induction of anesthesia with the use of a bronchoscope or with a video laryngoscope [10–12]. An alternative when securing the airway prior to placing a lung isolation device is the use of a laryngeal mask airway; with the aid of a flexible fiberoptic

Upper Airway Abnormalities and Lung Isolation

Patients requiring OLV can be identified during the preoperative evaluation to have a potentially difficult airway. This is in part because of the distorted airway anatomy caused by previous surgeries, radiation therapy, or both. Distorted anatomy may be found in the upper airway (tongue, pharynx, larynx). Various methods are available to provide lung isolation under these circumstances. The first step is to establish an airway with a single-lumen endotracheal tube placed orally when the patient is awake.

Use of a Flexible Fiberoptic Bronchoscope During Awake Intubation

Patients undergoing an awake fiberoptic bronchoscopy must receive oxygen via nasal cannula and be monitored, including the use of pulse oximetry. All local anesthetics used via spray or aerosolizer should be quantified to avoid overdose or complications postlocal anesthetics administration, such as seizures or methemoglobinemia. Also, patients undergoing an awake intubation should receive an antisialog medication such as glycopyrrolate. A simple approach to anesthetize the posterior part of the tongue is to apply lidocaine 5% ointment to a tongue blade depressor and let the patient hold this in his or her mouth for about 5 min. After the tongue blade depressor is removed, the next step is to use a mucosal atomization device (MAD[®]) to spray the local anesthetic (lidocaine 4%, 10 mL) directly to the pharynx, larynx, and vocal cords. When the patient experiences a cough reflex, it is very likely that the anesthetic has entered the vocal cords. The next step is to suction all residual secretions that were accumulated in the airway. In order to test that the gagging reflex is abolished, a Berman[®] intubating pharyngeal airway impregnated with lidocaine 5% ointment at the posterior tip end of the canula is advanced in the middle of the tongue until it is completely inserted in the oral cavity. The advantage of using the Berman[®] canula is that it facilitates a view of the epiglottis and allows the direct passage of the fiberscope followed by a single-lumen endotracheal tube. Also, the cannula protects the fiberscope against damage from the patient's teeth.

The fiberscope must be positioned in the midline such that the single-lumen endotracheal tube faces posteriorly during the attempt for intubation. In some cases, retraction of the single-lumen endotracheal tube and 90° counterclockwise rotation will facilitate passage of the tube through the vocal cords. Sometimes it is necessary to complement the local anesthetic with an additional dose of lidocaine 4% (3 mL) through the suction channel of the fiberscope to abolish the cough reflex during manipulation of the airway. The best indicator of proper placement of the fiberscope and the single-lumen endotracheal tube within the patient's trachea is the direct visualization of the tracheal rings and tracheal carina with the fiberscope along with the view of the tip of the single-lumen endotracheal tube inside the trachea [14]. Once the patient is intubated with a single-lumen endotracheal tube, then an independent bronchial blocker should be considered to achieve OLV.

Common independent bronchial blockers used through a single-lumen endotracheal tube include the following: a wire guided endobronchial Arndt[®] blocker sizes 5.0, 7.0, and 9.0 F [15], the Cohen[®] Flexitip blocker size 9.0 F [16], and the Fuji Uniblocker[®] sizes 4.5 and 9.0 F [17, 18] (see Chap. 16).

If a patient cannot open his/her mouth due to previous surgery and cannot be intubated orally, then an awake nasotracheal intubation can be performed taking all precautions of a nasal intubation, including the application of a vasoconstrictor followed by a local anesthetic and the passage of a single-lumen endotracheal tube. Once the airway is established, then



FIG. 17.3. A patient with previous hemimandibulectomy requiring nasotracheal intubation with an 8.0-mm internal diameter single-lumen endotracheal tube and an Arndt[®] blocker.

an independent bronchial blocker can be advanced [19, 20]. Figure 17.3 shows a patient with previous hemimandibulectomy requiring nasotracheal intubation with an 8.0 mm internal diameter single-lumen endotracheal tube and an Arndt[®] blocker passed through the multiport connector.

When an independent bronchial blocker is used, specifically size 9.0 F (the smallest acceptable single-lumen endotracheal tube size recommended is 8.0 mm internal diameter), it is important to have enough space between the bronchial blocker and the flexible fiberoptic bronchoscope so that navigation can be achieved with the single-lumen endotracheal tube. Once the single-lumen endotracheal tube is secured in the patient's trachea, an independent bronchial blocker can be advanced with the aid of a flexible fiberoptic bronchoscope. An advantage of the Cohen[®] or the Fuji Uniblocker[®] over the Arndt[®] wire-guided endobronchial blocker is that while advancing it to a desired bronchus, the distal tip of the blocker can be seen while entering a bronchus. With the Arndt blocker, the distal tip is looped into the fiberscope and cannot be seen until disengagement occurs. To achieve OLV the bronchial blocker must be advanced to the bronchus where lung collapse is required. One of the advantages of one-time intubation with a single-lumen endotracheal tube in a patient with a difficult airway is that it allows for the conversion to OLV with insertion of an independent bronchial blocker and simple removal of the blocker at the end of the procedure if postoperative ventilatory support is needed [21]. Once the blocker is within the targeted bronchus and the patient is turned into the lateral decubitus position, the endobronchial balloon is inflated. One of the multiple advantages of the newest bronchial blockers is that they have high-volume, low-pressure characteristics [22].

The amount of air needed to achieve a complete seal within the bronchus in an adult ranges between 5 and 8 mL of air. The optimal position of a bronchial blocker in the left or right bronchus is when the blocker balloon's outer surface is seen at least 10 mm below the tracheal carina inside the blocked

bronchus and a proper seal is achieved. Figure 17.4 shows the optimal position of an independent bronchial blocker through a single-lumen endotracheal tube.

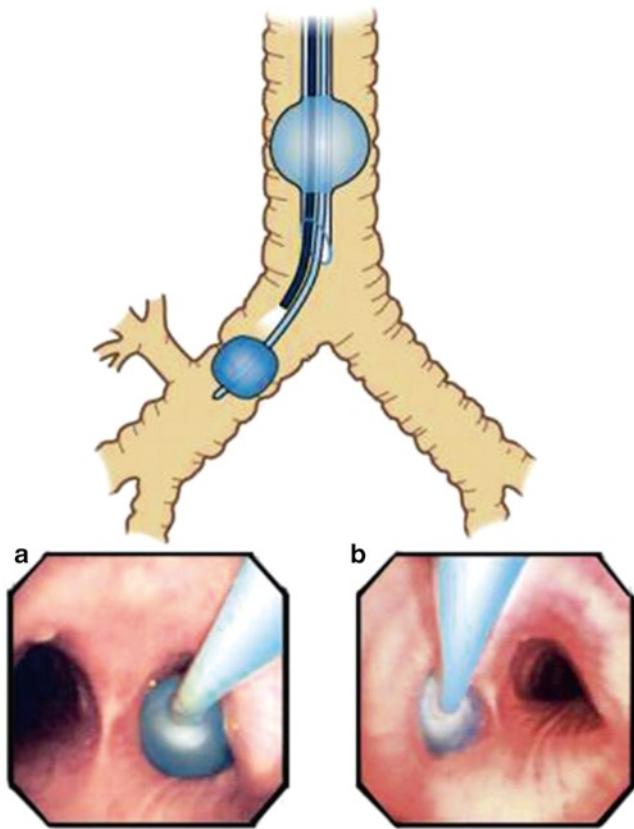


FIG. 17.4. The optimal position of an independent bronchial blocker through a single-lumen endotracheal tube. (a) The bronchial blocker balloon fully inflated into the right mainstem bronchus. (b) Fully inflated balloon in the entrance of the left mainstem bronchus [14].

Use of Laryngeal Mask Airway and a Bronchial Blocker During Difficult Airways

An alternative to achieve OLV in a patient with a difficult airway is with the use of a laryngeal mask airway in conjunction with the use of an independent bronchial blocker. A modified laryngeal mask airway can be made in which the aperture bar of the mask is removed to facilitate passage and insertion of a flexible fiberoptic bronchoscope and an Arndt® blocker in a patient with a recent tracheostomy in whom the laryngeal mask airway was placed orally [23]. In addition, the use of a ProSeal laryngeal mask airway has been used with a bronchial blocker in patients in whom the airway was deemed difficult and who required OLV during thoracoscopic surgery [24, 25].

Use of a Double-Lumen Endotracheal Tube in Patients with Difficult Airways

Intubation with a DLT can be more difficult than intubation with a single-lumen endotracheal tube. The larger size, the rigidity, and the shape of the DLT, without a bevel at the tip of the tube, can obscure the view of the glottis. In practice there are three different ways to place a DLT in a patient with a difficult airway. The first involves the use of airway topical anesthesia and awake fiberoptic bronchoscopy with passage of the flexible fiberoptic bronchoscope through the bronchial lumen of the DLT, where the tube is advanced under bronchoscopy guidance [26] (see Fig. 17.5). The second technique involves the use of ancillary lighted devices or video laryngoscopes that increase the visualization field of the epiglottis, vocal cords, and passage of the tube. The use of a malleable, lighted stylet (Mercury Medical, Clearwater, FL, USA) had been reported; it was used within the endobronchial lumen of the DLT, where the tip of the bulb was positioned distally at the tip of the DLT in patients with difficult airways [27].

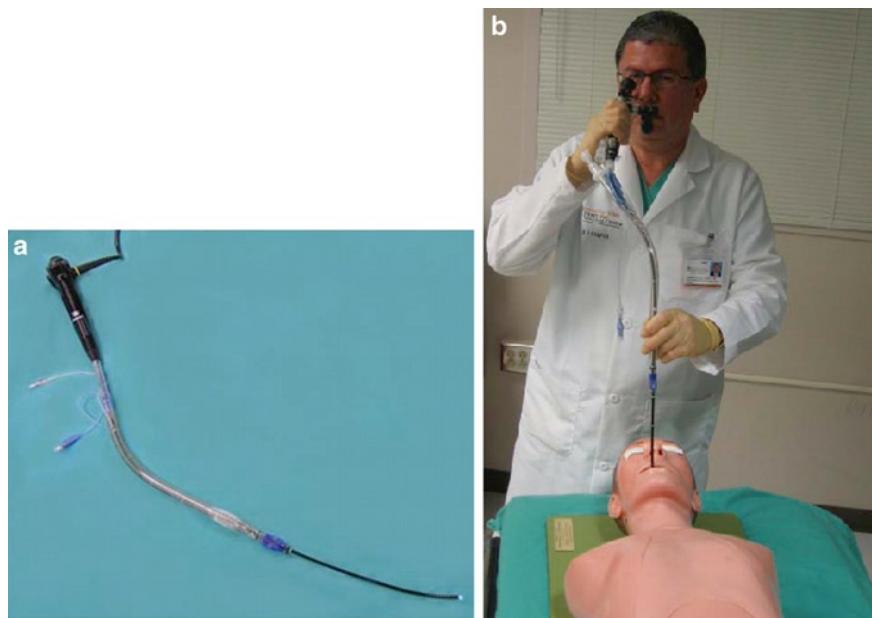


FIG. 17.5. (a) Pediatric fiberoptic bronchoscope passed through the endobronchial lumen of a double-lumen endotracheal tube (DLT) for fiberoptic intubation. Note that the actual working length of the DLT beyond the distal bronchial orifice is only approximately 20–25 cm. (b) Fiberoptic intubation of a mannequin with a left-sided DLT.

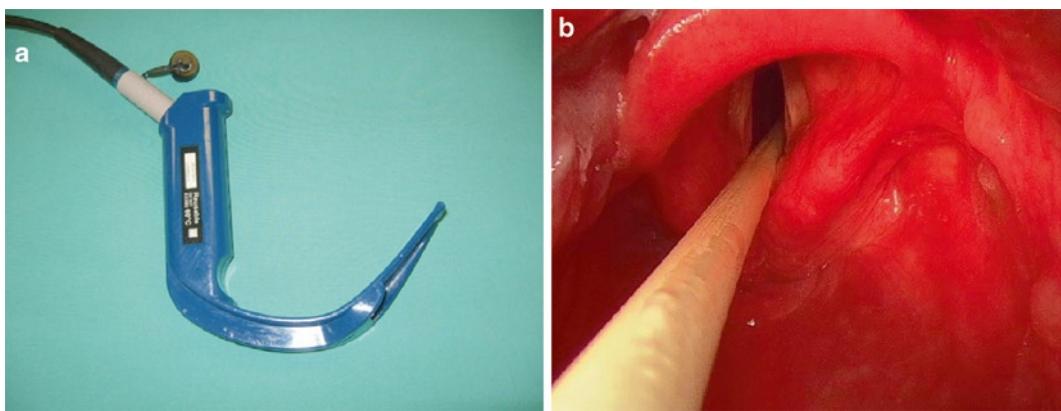


FIG. 17.6. (a) GlideScope® (Verathon Corp., Bothell, WA) video-laryngoscope. Note the acute flexion of the laryngoscope blade. (b) View of the glottis from a GlideScope® during a tube exchange. A tube exchange catheter can be seen passing through the vocal cords. This clear view of the glottis facilitates manipulation of the airway device during replacement of a single-lumen endotracheal tube with a DLT or vice versa.

Others have reported the use of a fiberoptic laryngoscope, the WuScope (Pentax Precision Instruments, Orangeburg, NJ, USA) during placement of a DLT in patients with abnormal airway anatomy [28]. One of the advantages of the fiberoptic laryngoscope is that it protects against rupture of the endotracheal cuff during laryngoscopy because the DLT is enclosed with the laryngoscope blade. A disadvantage of this device is the need for smaller sized DLTs, such as 35–37 F.

The Glidescope® video laryngoscope (Saturn Biomedical Systems, Burnaby, British Columbia, Canada) has been used in patients with a difficult airway during placement of a DLT [29]. Another alternative is to intubate the patient's trachea with a single-lumen endotracheal tube during an awake fiberoptic bronchoscopy or after induction of anesthesia, and then a tube exchange technique can be used to replace the existing tube for a DLT after general anesthesia is induced [13] (see Fig. 17.6).

For an airway exchange catheter to function, it must have a hollow center channel and universal adapters to insufflate oxygen. The exchange catheter must have a flexible tip distally to avoid airway lacerations, be long in length, and have outer markings to control the depth of insertion while in use. For a DLT, the exchange catheter should be at least 83 cm long. The airway Aintree tube exchanger (Cook® Critical Care, Bloomington, IN, USA) has a large internal diameter that allows fiberoptic bronchoscopy guidance. Also, a 14 F airway exchange catheter can be used to facilitate insertion of 39 and 41 F DLTs. For a 35 or 37 F DLT, an 11 F airway exchange catheter can be used [29] (see Fig. 17.7).

The airway exchange catheter, single-lumen endotracheal tube, and the DLT combination should be tested in vitro before the exchange [30]. A sniffing position will facilitate tube exchange. After the airway exchange catheter is lubricated, it is advanced through a single-lumen endotracheal tube. The airway catheter should not be inserted deeper than 24 cm from the lips to avoid accidental rupture of laceration of the trachea, bronchi, or lung [31, 32]. After cuff deflation, the single-lumen endotracheal tube is withdrawn. Then the endobronchial lumen



FIG. 17.7. The recently introduced Cook® airway catheter (Cook Critical Care, Bloomington, IN) for exchange between DLTs and a single-lumen endotracheal tube. This recent modification has a soft distal (purple) tip to attempt to decrease the risk of distal airway injury during tube exchange (right). The proximal stiffer green end (left) has detachable connectors for emergency ventilation. Shown is the standard 15-mm outside diameter breathing circuit connector. The exchange catheter also comes with a jet ventilation connector (not shown).

of the DLT is advanced over the exchange catheter. It is optimal to use a video laryngoscope during the tube exchange to guide the DLT through the glottis under direct vision [11, 33]. If a video laryngoscope is not available, then having an assistant perform a standard laryngoscopy during tube exchange partially straightens out the alignment of the oropharynx and glottis and facilitates the exchange. Proper final position of

Lung Isolation and Difficult Airway

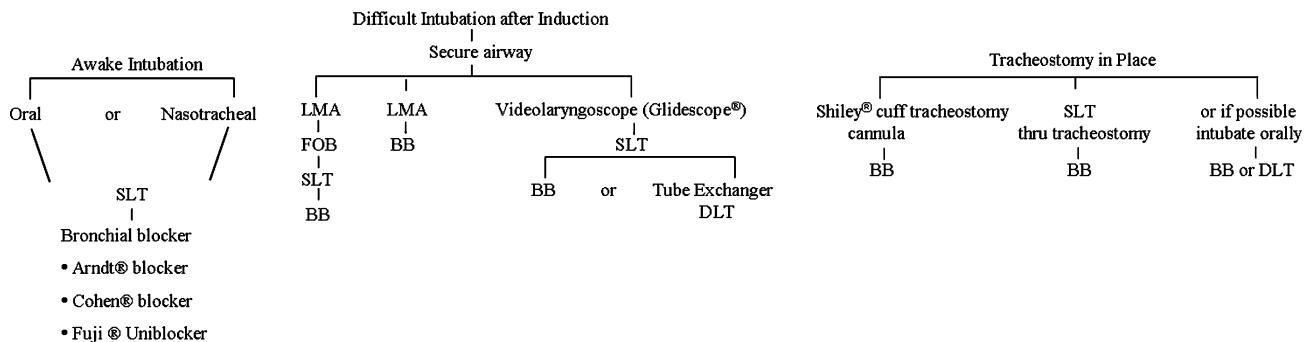


FIG. 17.8. Different alternatives to achieve lung isolation during difficult airways [10].

the DLT is then achieved with auscultation, presence of end tidal carbon dioxide (ETCO₂) wave form, and a fiberoptic bronchoscopy examination. Replacement of a DLT for a single-lumen endotracheal tube can be done at the conclusion of surgery with the use of a double airway exchange catheter. One study using two airway exchange catheters to exchange a DLT for a single-lumen endotracheal tube showed that there was a reduction in the incidence of glottis impingement of the tracheal tube and that there was a higher success rate of passage of the single-lumen endotracheal tube when compared with the use of a single airway exchange catheter [34]. The use of a double airway exchange catheter involves the following techniques: two 11 F, 83-cm-long airway exchange catheters from Cook® Critical Care are used. One catheter is passed through the endobronchial lumen of the DLT, making sure that the tip of the airway exchanger does not protrude distally in the tip of the DLT. A second exchange catheter is passed through the tracheal lumen; both wires provide easy placement of the new single-lumen endotracheal tube because of the increase rigidity with the two tube exchangers. For this technique to work, an 8.0-mm internal diameter single-lumen endotracheal tube must be used. Another variation of the tube exchanger technique is using a double-diameter coaxial airway exchange catheter. This consists of a 4.0-mm outer diameter exchanger inside a 7.0-mm outer diameter exchanger. This device allows for a more rigid guide-wire for replacing DLT with a single-lumen endotracheal tube. During tube exchanger techniques, it is recommended to use a video laryngoscope to visualize the proper exchange and move the tongue away from the tube. Figure 17.8 displays the different techniques to manage the patient who has a difficult airway and requires lung isolation. Several other manufacturers have introduced different designs



FIG. 17.9. Photograph of the Video MACINTOSH® System (Karl Storz, Culver City, CA) during intubation. Note the poor grade of view of the glottis seen with “line-of-sight” (photo is courtesy of Dr. R. Purugganan).

of video laryngoscopes that are also useful for lung isolation with difficult airways (see Fig. 17.9).

Lung Isolation Techniques in Patients with Tracheostomies

Before placing any lung isolation devices through a tracheostomy stoma, it is important to consider whether it is a fresh stoma (i.e., few days old, when the airway can be lost immediately or decannulation can occur) versus a long-term

tracheostomy. A standard DLT placed through a tracheostomy stoma can be prone to malposition because the upper airway has been shortened and a conventional DLT is too long.

When selecting a DLT as a replacement of the tracheostomy cannula, a specially designed short version of a DLT such as the Naruke DLT can be used through the tracheostomy stoma. In a report involving six patients with permanent tracheostomies, the Naruke tube was used with satisfactory results in patients requiring thoracic surgery and OLV [35].

An alternative to DLT placement to achieve OLV in a tracheostomized patient includes the following: insertion of a single-lumen endotracheal tube followed by an independent bronchial blocker through the tracheostomy stoma [36], or

if possible oral access to the airway for standard placement of a single-lumen endotracheal tube followed by a bronchial blocker. Another option is the use of a disposable cuff tracheostomy cannula with an independent bronchial blocker passed coaxially. In these cases, a small-size fiberoptic bronchoscope (i.e., 3.5-mm outer diameter) is recommended. Figure 17.10 shows lung isolation in a patient with a small tracheal stoma. The tracheostomy device has been replaced; a small laryngeal mask airway LMA #3 has been used to ventilate the patient through the stoma. Also shown in the picture is a patient with a tracheostomy stoma where a 7.0-mm internal diameter single-lumen endotracheal tube has been advanced through the stoma followed by an Arndt® bronchial blocker.



FIG. 17.10. Shows lung isolation in a patient with a small tracheal stoma. The tracheostomy device has been replaced; to the *left* a small laryngeal mask airway LMA #3 has been used to ventilate the patient through the stoma. To the *right*, is shown a patient with a stoma where a 7.0-mm internal diameter single-lumen endotracheal tube has been advanced through the stoma followed by an Arndt® bronchial blocker.

Lower Airway Abnormalities and Lung Isolation

When dealing with the difficult airway and OLV, one important group of patients to consider include those patients who present with lower airway abnormalities, specifically distal trachea or bronchial lesions. The common problems that will preclude or contraindicate the use of a left-sided DLT include an intraluminal tumor of the left mainstem bronchus or a descending thoracic aortic aneurysm that compresses the entrance of a left mainstem bronchus. One option in these cases is to use a right-sided DLT guided with flexible fiberoptic bronchoscopy [37].

Another group of patients that has lower airway abnormalities and require OLV are patients with previous lobectomy; sometimes in these cases the distorted anatomy may contribute to difficulties in recognizing the right and left bronchi because of the loss of anatomical landmarks [38]. In these patients, a complete fiberoptic bronchoscopy exam of the trachea and bronchi prior to placement of lung isolation device is required in order to properly identify the anatomy of the tracheobronchial tree. Another lower airway abnormality includes the patient that has a diagnosis of tracheal–esophageal fistula. In these cases, the use of two small endotracheal tubes as endobronchial tubes placed under flexible fiberoptic bronchoscopy guidance can be used to secure the airway under these circumstances as shown in Fig. 17.11.

Lung Isolation in Patients with Cervical Spine Abnormalities

Injuries to the cervical spine occur in only 2–3% of all patients with blunt trauma but are significant because of their high level

of associated mortality and morbidity [39, 40]. Some of these patients have experienced trauma to the chest with an injury to the descending thoracic aorta. In these trauma patients, the atlantoaxial region is the most common site of injury and the sixth and seventh vertebrae are involved in over one-third of all injuries [41]. In these patients, all precautions must be taken with regard to cervical spine injury [42]. When such patients arrive for emergency surgery (i.e., repair of a descending thoracic aortic aneurysm), some are already intubated and have a Philadelphia cervical collar in place. If the patient requires lung isolation and is already intubated, a complete fiberoptic bronchoscopy exam must be done to assess injuries to the trachea or bronchus. Once the airway has been assessed, then the use of an independent blocker through the single-lumen endotracheal tube is recommended. A Fuji Uniblocker® or Cohen® blocker is desirable because during the insertion it is easier to observe the tip of the blocker as it is guided into the left mainstem bronchus. Once the surgery is completed and lung isolation is no longer needed, removal of the bronchial blocker at the conclusion of the case allows the patient to remain intubated with the existing single-lumen endotracheal tube.

Bronchial blockers are often the best option for lung isolation in patients with cervical spine instability due to medical conditions such as Rheumatoid Arthritis (see Fig. 17.12).

Extubation or Mechanical Ventilation After Surgery

Extubation at the completion of surgery in a patient who has a difficult airway represents a challenge. Factors to consider prior to extubation include any mucosal edema, bleeding or lacerations to the pharynx during intubation, the length of surgery, and the amount of fluid administered during the intraoperative

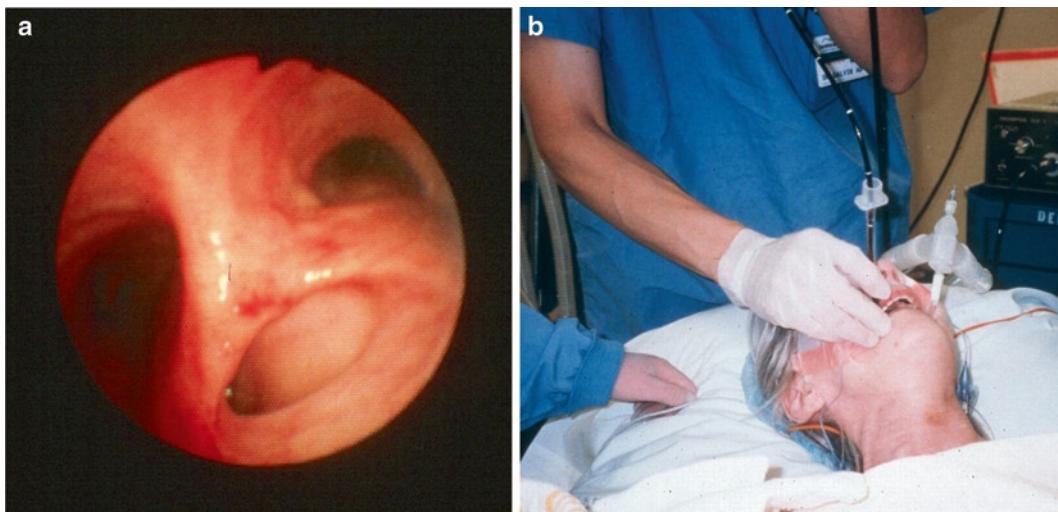


FIG. 17.11. (a) Fiberoptic bronchoscopic photograph of a tracheoesophageal fistula caused by esophageal cancer. The fistula is seen posteriorly at the level of carina at 5 o'clock. The left mainstem bronchus is at 9 o'clock, and the right mainstem bronchus is at 2 o'clock. (b) Fiberoptic-guided placement of bilateral endobronchial tubes (5-mm internal diameter microlaryngoscopy tubes) for repair of tracheoesophageal fistula in the same patient (photos are courtesy of Dr. R Grant).



FIG. 17.12. This patient with rheumatoid arthritis has a retroflexed odontoid process and associated inflammatory mass (pseudogout) causing compression of the cervical spinal cord just inferior to the foramen magnum. The patient also had intervertebral subluxations and osteophytes from C3 to C5 that cause cord compression. The anesthetic plan included an awake fiberoptic intubation with a single-lumen endotracheal tube.

period. Continuous access to the airway should be maintained in case reintubation is needed. The single-lumen endotracheal tube or the DLT can be removed with an airway catheter exchanger in place prior to extubation [43].

In some instances in a patient with a difficult airway and a DLT may require mechanical ventilation in the postoperative period. One option for extubation of these patients is to deflate both cuffs, withdraw the tube above the carina, then reinflate the tracheal cuff, and convert the DLT to two-lung ventilation [44], particularly if the conversion to exchange a DLT for a single-lumen endotracheal tube is considered too risky.

Another alternative technique is to exchange a DLT for a single-lumen endotracheal tube using an airway catheter exchanger under direct vision with a laryngoscope [45] or video laryngoscope [46–48].

Summary

In patients who require OLV, a key element during the preoperative assessment is the recognition and identification of the potentially difficult airway. The safest way to establish an airway is by securing the airway with a single-lumen endotracheal tube placed orally or nasotracheally with the aid of flexible fiberoptic bronchoscopy. Lung isolation in these patients

is achieved best with the use of an independent bronchial blocker. An alternative can be the use of a DLT with an airway catheter exchange technique. For the patient who has a tracheostomy in place, the use of an independent bronchial blocker through a single-lumen endotracheal tube or through a tracheotomy cannula in place is recommended. For all these devices, a flexible fiberoptic bronchoscopy examination is recommended prior, during placement, and at the conclusion of the use of lung isolation devices.

Clinical Case Discussion

Case: A 61-year-old male with a left-upper lobe lung mass is scheduled for a left-upper lobectomy. He is 175 cm tall and weighs 93 kg. Relevant history includes right maxillary mucoepidermoid carcinoma resected by radical neck surgery in the past, with additional radiation therapy and reconstruction using a right radial forearm flap; his tobacco history is that he smoked two packs of cigarettes per day for 40 years.

Airway exam reveals the following: full dentures. Mallampati score III, thyromental distance two finger breadths, neck range of motion very limited, and scarring from maxillary resection and radiation. Palpation of the anterior neck shows a hard and rigid consistency tissue. Also, the mouth is distorted and deviated towards the right side.

Questions

- What technique would you select to intubate this patient?
- What potential problems do you expect during an awake fiberoptic bronchoscopy in a patient with a previous neck resection and extensive surgery?
- What device and size would you use to provide lung isolation?
- What are the common problems in the intraoperative period with the use of bronchial blockers?
- What are the complications associated with the bronchial blocker?
- What are the advantages and disadvantages of using a bronchial blocker during a case with a difficult airway that requires lung isolation?

The Key Is to Focus on Patient's Anatomy in Order to Select the Lung Isolation Device

- Review the chest radiograph to appreciate the distorted tracheobronchial anatomy.
- Focus on lung isolation devices during difficult airways.
- Familiarity with the use of independent blockers (Arndt®, Cohen®, and Fuji Uniblocker®) is mandatory.
- Skills with flexible fiberoptic bronchoscopy during awake intubation, as well as during placement of bronchial blockers, are essential.

Expected Intraoperative Problems with the Use of Bronchial Blockers

- High incidence of malpositions.
- A balloon of the bronchial blocker can occlude the trachea and produce cardiopulmonary collapse if dislodged.

Suggested Management

In patients requiring OLV who are identified during the preoperative evaluation to have difficult airway as in the case presented here, the main challenges include: (1) to safely secure the airway and (2) to select the proper bronchial blocker to achieve lung isolation during OLV. The main problem in this case is to safely establish an airway because of previous neck surgery that distorted his airway anatomy. An awake flexible fiberoptic bronchoscopy was used. After airway topical anesthesia was achieved, a fiberoptic bronchoscope was passed orally with a guided 8.5-mm internal diameter single-lumen endotracheal tube. Bronchoscopy showed that the upper airway was severely distorted; a deviation of the larynx towards the right side and bulging scar tissue from previous surgery.

A single-lumen endotracheal tube was advanced without difficulty. After the tube was secured, a complete fiberoptic bronchoscopy exam was achieved with general anesthesia. The second issue described in this case was to achieve successful lung isolation. It was done with a 9 F Arndt® blocker that was passed under direct fiberoptic bronchoscopy into the left-mainstem bronchus. The optimal position was confirmed in the lateral decubitus position. After completion of the left upper lobectomy, two-lung ventilation was reestablished, the bronchial blocker was withdrawn, and the patient was extubated without any complications.

References

1. Campos JH. Progress in lung separation. *Thorac Surg Clin*. 2005;15:71–83.
2. Hagiwira S, Takashina M, Mori T, Yoshiya I. One-lung ventilation in patients with difficult airways. *J Cardiothorac Vasc Anesth*. 1998;12:186–8.
3. Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic anesthesia. *Curr Opin Anaesthesiol*. 2009;22:4–10.
4. Boiselle PM. Imaging of the large airways. *Clin Chest Med*. 2008;29:181–93.
5. Seymour AH. The relationship between the diameters of the adult cricoid ring and main tracheobronchial tree: a cadaver study to investigate the basis for double-lumen tube selection. *J Cardiothorac Vasc Anesth*. 2003;17:299–301.
6. Minnich DJ, Mathisen DJ. Anatomy of the trachea, carina and bronchi. *Thorac Surg Clin*. 2007;17:571–85.
7. Stene R, Rose M, Weigner MB, et al. Bronchial trifurcation at the carina complicating use of a double-lumen tracheal tube. *Anesthesiology*. 1994;80:1162–4.
8. American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2003;98:1269–77.
9. Campos JH. Difficult airway and one-lung ventilation. *Curr Rev Clin Anesth*. 2002;22:199–205.
10. Campos JH. Lung isolation techniques for patients with difficult airways. *Curr Opin Anaesthesiol*. 2010;23:12–7.
11. Poon KH, Liu EH. The airway scope for difficult double-lumen tube intubation. *J Clin Anesth*. 2008;20:319.
12. Davis L, Cook-Sather SD, Schreiner MS. Lighted stylet tracheal intubation: a review. *Anesth Analg*. 2000;90:745–6.
13. Perlin DI, Hannallah MS. Double-lumen tube placement in a patient with a difficult airway. *J Cardiothorac Vasc Anesth*. 1996;10:787–8.
14. Campos JH. Fiberoptic bronchoscopy in anesthesia. *Curr Rev Clin Anesth*. 2008;29:61–72.
15. Arndt GA, Buchika S, Kraner PW, DeLessio ST. Wire-guided endobronchial blockade in a patient with a limited mouth opening. *Can J Anaesth*. 1999;46:87–9.
16. Cohen E. The Cohen flexitip endobronchial blocker: an alternative to a double lumen tube. *Anesth Analg*. 2005;101:1877–9.
17. Campos JH. Which device should be considered the best for lung isolation: double-lumen endotracheal tube versus bronchial blockers. *Curr Opin Anaesthesiol*. 2007;20:27–31.
18. Narayanaswamy M, McRae K, Slinger P, et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. *Anesth Analg*. 2009;108:1097–101.
19. Campos JH. Use of the wire-guided endobronchial blocker for one-lung anesthesia in patients with airway abnormalities. *J Cardiothorac Vasc Anesth*. 2003;17:352–4.
20. Angie Ho CY, Chen CY, Yang MW, Liu HP. Use of the Arndt wire-guided endobronchial blocker via nasal for one-lung ventilation in patient with anticipated restricted mouth opening for esophagectomy. *Eur J Cardiothorac Surg*. 2005;28:174–5.
21. Cohen E. Pro: the new bronchial blockers are preferable to double-lumen tubes for lung isolation. *J Cardiothorac Vasc Anesth*. 2008;22:920–4.
22. Roscoe A, Kanellakos GW, McRae K, Slinger P. Pressures exerted by endobronchial devices. *Pressures exerted by endobronchial devices*. *Anesth Analg*. 2007;104:655–8.
23. Robinson III AR, Gravenstein N, Alomar-Melero E, Peng YG. Lung isolation using a laryngeal mask airway and a bronchial blocker in a patient with a recent tracheostomy. *J Cardiothorac Vasc Anesth*. 2008;22:883–6.
24. Ozaki M, Murashima K, Fukutome T. One-lung ventilation using the ProSeal laryngeal mask airway. *Anaesthesia*. 2004;59:726.
25. Tsuchihashi T, Ide S, Nakagawa H, Hishinuma N, et al. Differential lung ventilation using laryngeal mask airway and a bronchial blocker tube for a patient with unanticipated difficult intubation. *Masui*. 2007;56:1075–7.
26. Patane PS, Sell BA, Mahla ME. Awake fiberoptic endobronchial intubation. *J Cardiothorac Anesth*. 1990;4:229–31.
27. O'Connor CJ, O'Connor TA. Use of lighted stylets to facilitate insertion of double-lumen endobronchial tubes in patients with difficult airway anatomy. *J Clin Anesth*. 2006;18:616–9.

28. Smith CE, Karet M. Fiberoptic laryngoscopy (WuScope) for double-lumen endobronchial tube placement in two difficult-intubation patients. *Anesthesiology*. 2000;93:906–7.
29. Hernandez AA, Wong DH. Using a Glidescope for intubation with a double lumen endotracheal tube. *Can J Anaesth*. 2005;52:658–9.
30. Benumof JL. Difficult tubes and difficult airways. *J Cardiothorac Vasc Anesth*. 1998;12:131–2.
31. Thomas V, Neustein SM. Tracheal laceration after the use of an airway exchange catheter for double-lumen tube placement. *J Cardiothorac Vasc Anesth*. 2007;21:718–9.
32. deLima LG, Bishop MJ. Lung laceration after tracheal extubation over a plastic tube changer. *Anesth Analg*. 1991;73:350–1.
33. Chen A, Lai HY, Lin PC, Chen TY, Shyr MH. GlideScope-assisted double-lumen endobronchial tube placement in a patient with an unanticipated difficult airway. *J Cardiothorac Vasc Anesth*. 2008;22:170–2.
34. Suzuki A, Uraoka M, Kimura K, Sato S. Effects of using two airway exchange catheters on laryngeal passage during change from a double-lumen tracheal tube to a single-lumen tracheal tube. *Br J Anaesth*. 2007;99:440–3.
35. Saito T, Naruke T, Carney E, et al. New double intrabronchial tube (Naruke tube) for tracheostomized patients. *Anesthesiology*. 1998;89:1038–9.
36. Tobias JD. Variations on one-lung ventilation. *J Clin Anesth*. 2001;13:35–9.
37. Campos JH, Ajax TJ, Knutson R, et al. Case conference 5–1990. A 76-year-old man undergoing an emergency descending thoracic aortic aneurysm repair has multiple intraoperative and postoperative complications. *J Cardiothorac Anesth*. 1990;4:631–45.
38. Campos JH. Update on selective lobar blockade during pulmonary resections. *Curr Opin Anaesthesiol*. 2009;22:18–22.
39. Hoffman JR, Schriger DL, Mower WR, et al. Low-risk criteria for cervical-spine radiography in blunt trauma: a prospective study. *Ann Emerg Med*. 1992;21:1454–60.
40. Roberge RJ, Wears RC, Kelly M, et al. Selective application of cervical spine radiography in alert victims of blunt trauma: a prospective study. *J Trauma*. 1988;28:784–8.
41. Goldberg W, Mueller C, Panacek E, et al. Distribution and patterns of blunt traumatic cervical spine injury. *Ann Emerg Med*. 2001;38:17–21.
42. Crosby ET. Airway management in adults after cervical spine trauma. *Anesthesiology*. 2006;104:1293–318.
43. Mort TC. Continuous airway access for the difficult extubation: the efficacy of the airway exchange catheter. *Anesth Analg*. 2007;105:1357–62.
44. Merlone SC, Shulman MS, Allen MD, Mark JB. Prolonged intubation with a polyvinylchloride double-lumen endobronchial tube. *J Cardiothorac Anesth*. 1987;1:563–4.
45. Benumof JL. Airway exchange catheters: simple concept, potentially great danger. *Anesthesiology*. 1999;91:342–4.
46. Merli G, Guarino A, Della Rocca G, et al. Recommendations for airway control and difficult airway management in thoracic anesthesia and lung separation procedures. *Minerva Anestesiol*. 2009;75:59–78.
47. Pott LM, Murray WB. Review of video laryngoscopy and rigid fiberoptic laryngoscopy. *Curr Opin Anaesthesiol*. 2008;21:750–8.
48. Thong SY, Lim Y. Video and optic laryngoscopy assisted tracheal intubation—the new era. *Anaesth Intensive Care*. 2009;37: 219–33.

18

Intraoperative Patient Positioning and Neurological Injuries

Cara Reimer and Peter Slinger

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Key Points

- Thoracic cases usually involve repositioning the patient after induction of anesthesia. Vigilance is required to avoid major displacement of airway devices, lines, and monitors during and after position changes.
- Obtaining central venous access after changing to the lateral position is extremely difficult. If a central line may be needed it should be placed at induction.
- Prevention of peripheral nerve injuries in the lateral position requires a survey of the patient from the head and sides of the operating table prior to draping.
- Postthoracotomy paraplegia is primarily a surgical complication.

Introduction

The majority of thoracic procedures are performed in the lateral position but depending on the surgical technique a flexed-lateral (nephrectomy), supine, semisupine, or semi-prone lateral position may be used. The lateral positions have specific implications for the anesthesiologist.

Position Change

It is awkward to induce anesthesia in the lateral position. Thus, monitors will be placed and anesthesia will usually be induced in the supine position and the anesthetized patient will then be repositioned for surgery. Sometimes multiple repositionings are required during a single case. It is possible to induce anesthesia in the lateral position and this may rarely be indicated with unilateral lung diseases such as bronchiectasis or hemoptysis until lung isolation can be achieved. However, even these patients will then have to be repositioned after induction and the diseased lung turned to the nondependent position. The operating room team, led by the anesthesiologist, needs to follow a standardized protocol to avoid injury to the patient and displacement of lines, tubes, and monitors during each position change.

Due to the loss of venous vascular tone in the anesthetized patient, it is not uncommon to see hypotension when turning the patient to or from the lateral position. All lines and monitors will have to be secured during position change and their function reassessed after repositioning. The anesthesiologist should take personal responsibility for the head, neck, and airway during position change and must be in charge of the

TABLE 18.1. Neurovascular injuries specific to the lateral position routine “head-to-toe” survey.

1. Dependent eye
2. Dependent ear pinna
3. Cervical spine in line with thoracic spine
4. Dependent arm
 - i. Brachial plexus
 - ii. Circulation
5. Nondependent arm^a
 - i. Brachial plexus
 - ii. Circulation
6. Dependent and nondependent suprascapular nerves
7. Nondependent leg sciatic nerve
8. Dependent leg
 - i. Peroneal nerve
 - ii. Circulation

^aNeurovascular injuries of the nondependent arm are more likely to occur if the arm is suspended or held in an independently positioned armrest

operating team to direct repositioning. It is useful to make an initial “head-to-toe” survey of the patient after induction and intubation checking oxygenation, ventilation, hemodynamics, lines, monitors, and potential nerve injuries. This survey then must be repeated and documented after repositioning (see Table 18.1). It is nearly impossible to avoid some movement of a double-lumen tube or bronchial blocker during repositioning [1]. The patient’s head, neck, and endobronchial tube should be turned “en-bloc” with the patient’s thoracolumbar spine. However, the margin of error in positioning endobronchial tubes or blockers is often so narrow that even very small movements can have significant clinical implications [2]. The carina and mediastinum may shift independently with repositioning and this can lead to proximal misplacement of a previously well-positioned tube. Endobronchial tube/blocker position and the adequacy of ventilation must be rechecked by auscultation and fiberoptic bronchoscopy after patient repositioning.

The Lateral Position (Also Referred to as the Lateral Decubitus Position)

This is the commonest position for thoracic surgical procedures. The patient may be positioned on a vacuum mat (see Fig. 18.1) or on cushions (see Fig. 18.2). The operating table headrest and pillows must be adjusted so that the cervical spine remains in-line with the thoracic spine. It is very easy after repositioning the patient in the lateral position to cause excessive lateral flexion of the cervical spine because of improper positioning of the patient’s head. This malpositioning, which exacerbates brachial plexus traction, can cause a “whiplash” syndrome and is difficult to appreciate from the head of the operating table, particularly after the surgical drapes have been placed. It is useful for the anesthesiologist to survey the patient from the side of the table immediately after turning to ensure that the entire vertebral column is aligned properly. Both eyes should be visible to the anesthesiologist throughout

the procedure to avoid compression on the globes by pillows or lines. The dependent ear pinna may be positioned in the center of a gel ring.

The dependent arm is positioned on an armrest at 90° to the table and the nondependent arm is positioned on an armrest or pillows. The brachial plexus is the site of the majority of intraoperative nerve injuries related to the lateral position [3]. These are basically of two varieties: the majority are compression injuries of the brachial plexus of the dependent arm but there is also significant risk of stretch injuries to the brachial plexus of the nondependent arm. The brachial plexus is fixed at two points: proximally by the transverse processer of the cervical vertebrae and distally by the axillary fascia. This two-point fixation plus the extreme mobility of neighboring skeletal and muscular structures makes the brachial plexus extremely liable to injury (see Table 18.2). The patient should be positioned with padding under the dependent thorax (see Fig. 18.2) to keep the weight of the upper body off the dependent arm brachial plexus. Unfortunately, this pad is called an “axillary pad” or “axillary-roll” in some institutions. However, this padding will exacerbate the pressure on the brachial plexus if it migrates superiorly into the axilla.

The brachial plexus of the nondependent arm is most at risk if it is suspended from an independently fixed arm support or “ether screen” (see Fig. 18.3). Traction on the brachial plexus in these situations is particularly likely to occur if the patient’s trunk accidentally slips towards a semiprone or semisupine position after fixation of the nondependent arm. Vascular compression of the nondependent arm in this situation is also possible and it is useful to monitor pulse oximetry in the nondependent hand to observe this. The arm should not be abducted beyond 90° and should not be extended posteriorly beyond the neutral position nor flexed anteriorly greater than 90°. Fortunately, the majority of these nerve injuries resolve spontaneously over a period of months.

Anterior flexion of the arm at the shoulder (circumduction) across the chest or lateral flexion of the neck toward the opposite side can cause a traction injury of the suprascapular nerve [4]. This causes a deep, poorly circumscribed, pain of the posterior and lateral aspects of the shoulder and may be responsible for some cases of postthoracotomy shoulder pain.

The dependent leg should be slightly flexed with padding under the knee to protect the peroneal nerve lateral to the proximal head of the fibula. The nondependent leg is placed in a neutral extended position and padding placed between it and the dependent leg. The dependent leg must be observed for vascular compression. Excessively tight strapping at the hip level can compress the sciatic nerve of the nondependent leg.

Flexed-Lateral Position

To lower the nondependent iliac crest so that it does not interfere with surgical access, most patients for VATS surgery are placed in a flexed-lateral position (see Fig. 18.4) similar to the nephrectomy position with lateral flexion of the lower thoracolumbar spine while the upper thoracic and cervical spine

FIG. 18.1. Patient in the lateral position on a vacuum mat. Note both arms are supported on armrests which are fixed to the operating table. This position of the arms allows good access to the head for monitoring and airway management after surgical draping. The dependent leg is straight and the nondependent leg flexed (with kind permission from Springer Science + Business Media: Aschemann [15]).



FIG. 18.2. Posterior view of a patient in the lateral view with cushions. It is very important to survey the patient from this perspective to ascertain that the cervico-thoracic spine is in alignment prior to draping. After turning from the supine position, it is very easy to accidentally reposition the patient with a degree of lateral cervical flexion that is difficult to appreciate from the head of the table. Note the extra padding under the upper thorax below the axilla. Also note the gel ring preventing compression of the dependent ear pinna and the cushioning between the legs (with kind permission from Springer Science + Business Media: Aschemann [15]).



TABLE 18.2. Factors contributing to brachial plexus injury in the lateral position.

- | |
|---|
| a. Dependent arm (compression injuries) |
| 1. Arm directly under thorax |
| 2. Pressure on clavicle into retro-clavicular space |
| 3. Cervical rib |
| 4. Caudal migration of thorax padding into the axilla ^a |
| b. Nondependent arm (stretch injuries) |
| 1. Lateral flexion of cervical spine |
| 2. Excessive abduction of arm (>90%) |
| 3. Semiprone or semisupine repositioning after arm fixed to a support |

^aUnfortunately, this padding under the thorax is misnamed an “Axillary roll” in some institutions. This padding absolutely should not be placed in the axilla

is maintained in a horizontal plane. Some surgeons also use this position for thoracotomies to try and open the intercostal spaces. After repositioning and stabilization, the hemodynamics of the lateral position are not significantly different from the supine position. However, the flexed-lateral position impairs venous return and is associated with significant reductions in blood pressure and cardiac index (3.0 vs. 2.4 L/min/m² in one study [5]). This can particularly be a problem in the elderly, who are more liable to have clinically important falls in blood pressure with decreases in preload.

Positive pressure ventilation during anesthesia in the lateral position is associated with significant increases in mismatching of ventilation and perfusion. These changes are discussed in Chap. 5.

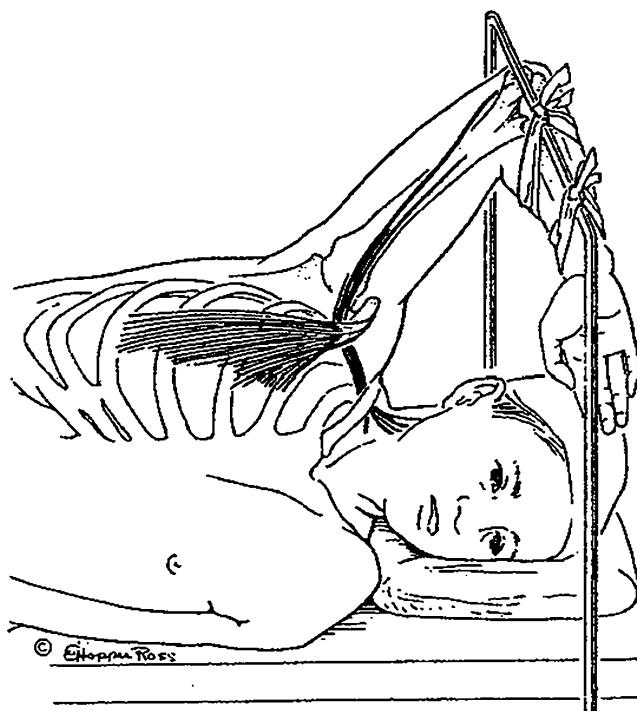


FIG. 18.3. Bilateral malpositioning of the arms in the lateral position. The nondependent arm is hyperextended and fixed to the anesthetic screen. This causes traction of the brachial plexus as it passes under the clavicle and the tendon of the pectoralis minor muscle. This traction may increase if the patient's torso rotates during surgery while the arm remains fixed. The dependent arm is directly under the thorax with the potential for vascular compression and/or injury to the brachial plexus (with kind permission from Springer Science + Business Media: Britt and Gordon [3], p. 9, Figure 5. ©E Hopper Ross).



FIG. 18.4. Posterior view of the flexed-lateral position commonly used for thoracoscopic (VATS) surgery. The patient is on a vacuum mat and a forced-air warmer has been applied to the lower body prior to draping. The flexed-lateral position is more likely to cause impairment of venous return and hypotension than the lateral position.

Supine Positions

The standard supine position with arms abducted is used for a variety of thoracic surgical procedures such as sternotomies for mediastinal tumors or bilateral wedge resections. The arms are positioned prone with careful attention to padding the ulnar nerves at the elbow to prevent pressure. The supine position with the arms abducted may be used for bilateral trans-sternal thoracotomies (the “clam-shell” incision) for bilateral lung transplantation or large anterior mediastinal mass resections or for bilateral thoracoscopic procedures (see Fig. 18.5). The arms are positioned supine and not abducted more than 90°. The arms should be padded with the joints slightly flexed, so that the wrist is higher than the elbow and the elbow higher than the shoulder.

Central Neurological Injuries

Paraplegia

With an estimated incidence of 0.08% [6], postthoracotomy paralysis (PTP) is a rare but devastating complication following thoracic surgery. PTP can occur as a result of spinal cord compression from an epidural hematoma (EH) or a foreign body, or ligation of major arteries perfusing the vulnerable thoracic cord. Arterial embolus and perioperative hypotension have also been implicated.

EH is a rare but well-appreciated complication of neuraxial anesthesia. EH associated with epidural placement is estimated to occur with a frequency of 1:150,000 [7]. Symptoms of EH vary, but can include back pain, sensory and motor deficits, and incontinence. EH can present any time, including immediately postoperatively and after catheter removal. Prompt diagnosis, ideally with MRI scanning, can confirm the

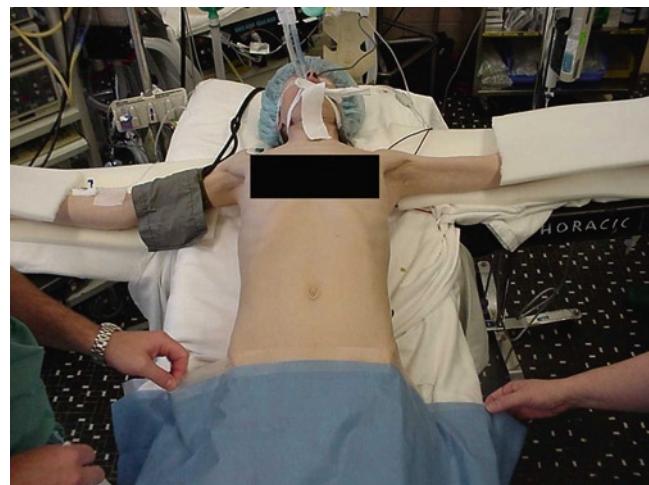


FIG. 18.5. The supine position with the arms abducted. This position is appropriate for bilateral thoracoscopic procedures or for bilateral lung transplantation.

diagnosis. Immediate neurosurgical consultation should be obtained for decompression which has its best results within 12 h of onset of symptoms [8].

Surgical bleeding at or near the costo-vertebral junction with postero-lateral thoracotomy incisions can be difficult to manage. There are multiple case reports [9] of oxidized cellulose polymer (Surgicel) positioned and left at or near the angle of the vertebral body to control bleeding. The material has subsequently swelled and compressed the ipsilateral nerve root, or even migrated into the spinal canal, causing permanent paralysis. The product monograph specifically contraindicates the use of the polymer in this situation. Neurologic deficit in this scenario presents within hours of surgery. Diagnosis is confirmed with imaging and treatment is removal.

Paralysis due to spinal cord ischemia is a commonly appreciated complication of vascular surgery, where its postoperative incidence can reach upwards of 20% [10]. Nonvascular thoracic surgery can also lead to spinal cord ischemia. Anatomical considerations related to this have been reviewed [11]. To briefly summarize, the thoracic spinal cord has a less luxurious blood supply than its cervical and lumbar counterparts. The cord is supplied by the solitary anterior spinal artery (ASA) which provides blood supply to the anterior 2/3 of the cord and the paired posterior spinal (PSA) arteries which supply the posterior 1/3. In the thoracic region, the ASA receives important contributions from a few variable radicular arteries which are branches of the posterior intercostal arteries. Ligation of small but integral intercostal arteries during thoracic surgery, leading to hypoperfusion and ischemia of the spinal cord has been implicated in PTP, both in lung resection and esophagectomy. The classic presentation of spinal cord ischemia from ASA supply interruption in the thoracic region is bilateral motor, pain, and temperature loss with maintenance of proprioception, the so-called Anterior Cord Syndrome. There may be associated autonomic dysfunction.

Treatment of ischemia due to inadvertent surgical interruption of spinal cord blood supply is guided by interventions driven at optimizing supply and demand to the cord. Commonly used strategies include maintaining a normal to supra-normal blood pressure with vaso-inopressors, an adequate hemoglobin, and steroid administration. It should be noted that none of these interventions have been rigorously proven to improve neurologic outcome and some, in particular steroid administration, are controversial. Spinal drains are commonly placed electively in thoracic aneurysm repair to optimize spinal cord perfusion, but this treatment has not been utilized in the PTP literature.

To conclude, postthoracotomy neurologic deficit is usually assumed to be an anesthetic complication related to epidural placement. Although anesthesiologists must always be vigilant and act quickly in these cases to image the spinal cord to rule out a hematoma, we must also remember the differential includes surgically related causes.

Blindness

Postoperative visual loss (POVL) has been infrequently reported following surgery in the lateral position. Similar to the POVL more often reported after surgery in the prone position, the risk factors include prolonged surgery, hypotension, massive transfusion, diabetes, and obesity [12]. The etiology in noncardiac surgery has been primarily due to posterior ischemic optic neuropathy. The perfusion pressure in the posterior portion of the optic nerve is directly related to mean arterial pressure and inversely related to venous drainage pressure. In one case report following spine surgery in the lateral position via VATS and open thoracotomy, the visual loss was complete in the dependent eye and partial in the nondependent eye suggesting the potential impact of venous drainage pressure [13]. Of note, this patient also had marked facial edema after the end of the case. Since there is no monitor available to assess the perfusion pressure in the optic nerve, prevention involves avoiding the treatable associated factors (hypotension and anemia), regular intraoperative observation of the face to assure that there is no direct pressure on the eyes, and careful neutral positioning of the cervical spine to avoid any compromise of venous drainage.

Other Position-Related Injuries

The lateral position has been reported to be associated with a variety of pressure-related injuries to the legs. These include myonecrosis, sciatic nerve palsy, and compartment syndromes [14]. The majority of these reports involve orthopedic procedures of long duration (>5 h). Increased vigilance for potential position-related injuries is required in long procedures.

Clinical Case Discussion

A 60-year-old woman presents for a left thoracotomy for left lower lobectomy for lung cancer. Past medical history includes a remote myocardial infarction with a preoperative ejection fraction of 40%, controlled hypertension, and diet-controlled diabetes mellitus. Regular medications are taken the morning of the OR, including metoprolol and aspirin 81 mg. A flexible epidural catheter with inner stainless steel coil wire is placed at T6/7 for postoperative analgesia. After an epidural test dose of 3 mL lidocaine 2%, an infusion of bupivacaine 0.1% plus hydromorphone 15 µg/mL is started at 5 cc/h. A central line is placed after induction. The operation is remarkable for intraoperative hypotension requiring dopamine and norepinephrine and brisk bleeding near the costovertebral junction. Immediately postoperatively, blood pressure is in the patient's normal range with no support, there is no motor deficit, and pain is well controlled. Six hours postoperatively, a nurse from the ward calls to report that the patient is complaining of bilateral lower extremity motor weakness.

1. What is the differential diagnosis?

At this point, the differential is wide and includes a motor block secondary to epidural local anesthetic solution, an intrathecal catheter, compression of the nerve roots or spinal cord from an EH or a foreign body, arterial embolus to a radicular artery, or a hypoperfusion state.

2. What should be done immediately?

Vital signs should be taken and documented, the epidural solution should be stopped and the catheter aspirated. A focused chart review should be undertaken with special note taken of any recently administered anticoagulants. The surgeon should be called and be advised of the problem. A complete neurological examination should be performed.

3. What does the initial assessment reveal?

The patient is awake and alert. Her blood pressure is 89/65 with a normal heart rate and oxygen saturation. No blood or CSF is aspirated through the catheter. She is unable to move her legs. She has loss of sensation to pain and temperature in both legs, but proprioception is intact. Thirty minutes after the epidural solution has been turned off, there is no change in her neurological status. The last documented INR is 1.29 5 h ago. The patient received subcutaneous heparin for DVT prophylaxis 1 h ago.

4. What should be done next? What bloodwork, imaging, and consults should be ordered?

Dopamine is started through the patient's central line to keep the blood pressure in her normal range (120/80) with continuous cardiac monitoring. "STAT" complete blood count and coagulation tests are drawn. There is hesitation to remove the epidural catheter in the context of a coagulation abnormality combined with recent heparin administration and aspirin. MRI is the preferred modality to diagnose an EH. However, the *in situ* epidural catheter is not permitted in the scanner. After consultation with the radiologist, the epidural is left in place and a CT is performed. Neurosurgery and neurology are called and made aware of the patient.

5. What is found on additional testing?

The CT shows no EH or mass. The hemoglobin is 90 g/L. Platelets are normal. INR is 1.21. The patient is seen by neurology and given a provisional diagnosis of spinal cord ischemia causing an anterior cord syndrome.

6. What else can be done?

The patient is moved to a step-down unit with continuous monitoring. Neurologic vitals are done every 4 h.

Dopamine is continued, and the patient is given 100 mg methylprednisolone IV q8 h \times 3 doses. Hemoglobin is maintained at 100 g/L. The epidural is removed 6 h after the last subcutaneous heparin dose. An MRI is then performed and is normal. Pain is controlled with hydromorphone intravenous PCA. Over the next 4 days, the patient gradually and completely recovers.

References

1. Desiderio DP, Burt M, Kolver AC, et al. The effects of endobronchial cuff inflation on double-lumen endobronchial tube movement after lateral positioning. *J Cardiothorac Vasc Anesth*. 1997;11:595–9.
2. Fortier G, Coté D, Bergeron C, et al. New landmarks improve the positioning of the left Broncho-Cath double-lumen tube: comparison with the classic technique. *Can J Anaesth*. 2001;48:790–5.
3. Britt BA, Gordon RA. Peripheral nerve injuries associated with anaesthesia. *Can Anaesth Soc J*. 1964;11:514.
4. Lawson NW. The lateral decubitus position. In: Marton JT, editor. *Positioning in anesthesia and surgery*. 2nd ed. Philadelphia: WB Saunders; 1987. p. 175.
5. Yokoyama M, Ueda W, Hirakawa M. Haemodynamic effects of the lateral decubitus position and the kidney rest lateral decubitus position during anaesthesia. *Br J Anaesth*. 2000;84:753–7.
6. Attar S. Paraplegia after thoracotomy: report of five cases and review of the literature. *Ann Thorac Surg*. 1995;59:1410–6.
7. Horlocker T. Regional anaesthesia in the anticoagulated patient: defining the risks (the second ASRA consensus conference on neuraxial anaesthesia and anticoagulation). *Reg Anesth Pain Med*. 2003;28:172–97.
8. Kreppel D. Spinal hematoma: a literature survey with metaanalysis of 613 patients. *Neurosurg Rev*. 2003;26:1–49.
9. Short H. Paraplegia associated with the use of oxidized cellulose in posterolateral thoracotomy incisions. *Ann Thorac Surg*. 1990;50:288–90.
10. Greenberg R. Contemporary analysis of descending thoracic and thoracoabdominal aneurysm repair: a comparison of endovascular and open techniques. *Circulation*. 2008;118:808–17.
11. Shamji M. Circulation of the spinal cord: an important consideration for thoracic surgeons. *Ann Thorac Surg*. 2003;76:315–21.
12. Newman NJ. Perioperative visual loss after nonocular surgeries. *Am J Ophthalmol*. 2008;145:604–10.
13. Heitz JW, Audu PB. Asymmetric postoperative visual loss after spine surgery in the lateral decubitus position. *Br J Anaesth*. 2008;101:380–2.
14. Cascio BM, Buchowski JM, Frassica FJ. Well-limb compartment syndrome after prolonged lateral decubitus positioning. *J Bone Joint Surg*. 2004;86:2038–40.
15. Aschermann D. *Positioning techniques in surgical applications*. New York: Springer; 2006.

Intraoperative Monitoring

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Key Points

- Continuous automated ST-segment analysis is especially important during thoracic surgery given the potential for cardiac ischemia, arrhythmias, pneumothorax, severe hypoxemia, and hemodynamic instability.
- Oxygenation during one-lung ventilation is determined by many factors including cardiac output, blood pressure, ventilation–perfusion matching, anesthetic effects on hypoxic pulmonary vasoconstriction, airway mechanics and reactivity, oxygen consumption, and preexisting pulmonary disease. Pulse oximetry with occasional intermittent arterial blood gas analysis provides warning of significant hypoxemia.
- The typical CO_2 vs. time waveform, displayed on most anesthesia monitors, has characteristic intervals that represent different physiologic events during ventilation.
- Continuous breath-by-breath spirometry (monitoring of inspiratory and expiratory volumes, pressures, and flows) enables the early detection of a mal-positioned double-lumen tube and can reduce the potential for ventilatory-induced lung injury by guiding the optimization of ventilatory settings.
- Invasive arterial pressure monitoring is commonly used to assess beat-by-beat blood pressure and it can also be used to derive functional hemodynamic information such as systolic pressure variation (SPV) and pulse pressure variation (PPV).
- SPV and PPV measure related aspects of cardiorespiratory interaction and these variables can predict the ability to increase cardiac output with volume loading better than central venous pressure or pulmonary artery occlusion pressure.
- Minimally-invasive hemodynamic monitoring (such as the Esophageal Doppler, Arterial Pressure waveform-based devices, and/or central venous oximetry) coupled with goal-directed therapy care can improve outcomes by focusing on basic clinical questions such as: “is flow (cardiac output) adequate to meet global tissue demands?”

Introduction

The general principles of intraoperative monitoring for thoracic surgery are similar to those for any major surgery. Monitoring guides the detection of problems and helps track the response to interventions. From a practical standpoint, this translates into the rather conservative approach of invasive monitoring from the outset, with the assumption that cardiac and pulmonary complications are more prone to occur (relative to other noncardiac procedures), and that access to the patient may be restricted (especially with the patient in the lateral decubitus position during lung isolation).

Monitoring techniques have rarely been subjected to the kind of scrutiny that pharmacologic and other therapeutic interventions are [1]. With improvements in monitoring technology and in our understanding of cardiorespiratory physiology, we hope to acquire and interpret data better, recognize errors, generate and apply evidence-based goal-directed interventions to optimize outcomes in a cost-effective manner. Although this is self-evident, intraoperative monitoring, no matter how sophisticated, cannot *itself* improve outcomes. Monitoring coupled with physiologically-derived protocol-driven care can improve outcomes by reducing unwarranted variation in practice while still allowing practitioners to use their clinical judgment [2]. For instance, protocol-driven goal-directed resuscitation in septic patients has been shown to reduce mortality [3] while invasive Pulmonary Artery Catheter (PAC)-based monitoring during high-risk surgery has, in fact, been shown *not* to lead to better outcomes [4]. We will focus on intraoperative monitoring specifically relevant to thoracic surgical patients and will also emphasize minimally- and noninvasive hemodynamic monitoring technologies.

ECG

Approximately 30% of patients exposed to anesthesia for surgical procedures in the United States have a known prior history of coronary artery disease (CAD) or coronary risk factors. Perioperative myocardial ischemia is more common in patients with poor cardiopulmonary reserve that typically present for thoracic surgery. Multi-vessel coronary disease is also more likely in the thoracic surgical population given their likelihood of being smokers and having related comorbidities [5]. An estimated 50,000 such patients per year, who receive noncardiac surgery, will experience a perioperative myocardial infarction, which carries a 40–70% mortality rate.

Continuous automated ST-segment analysis is fundamental during thoracic surgery due to the potential for cardiac ischemia as a result of arrhythmias, pneumothorax, the potential for severe hypoxemia from intrapulmonary shunting, and hemodynamic instability from the compression of large vessels with the potential for cardiac decompensation from pulmonary hypertension or hemorrhage [6]. The typical

five-lead electrocardiographic system should be placed for thoracic surgical patients with suspected or known coronary disease undergoing thoracic surgery. Depending on the surgical site, careful positioning of leads is pivotal in order to both avoid errors in the ST-segment analysis and minimize interference with the sterile surgical field. Based on previous studies, lead II has a 90% sensitivity to detect arrhythmias and the lateral lead V5 has 75% sensitivity to detect lateral wall ischemia. London M, et al. (Anesthesiology 1988;69:232–41) demonstrated that lead V4 was the second-most sensitive lead to detect intraoperative ischemia (61% sensitivity) and that the use of two lateral leads (V4 and V5) provided a combined sensitivity of 90% for the detection of lateral wall ischemia. ST-segment trend analysis is pivotal for the diagnosis of myocardial ischemia caused by and characteristic of multi-vessel coronary disease in patients with a significant history of smoking and with poor collateral circulation [7]. Specific coronary artery territories typically implicated in ischemia or infarction can be diagnosed based on the congruence of leads showing ST-segment changes (for instance, changes in leads II, III and aVF typically represent RCA territory supply/demand mismatch). Although the diagnosis of acute MI in the presence of a Left Bundle Branch Block (LBBB) is difficult, criteria have been developed that may be applied for early detection and timely intervention [8].

ECG can also be used to monitor for various severe electrolyte disturbances (e.g., hyperkalemia, hypocalcemia, hypomagnesaemia) and the appropriate functioning of Cardiac Rhythm Management Devices. As a result of serious underlying cardiac rhythm disturbances or congestive heart failure, many patients undergoing thoracic surgery will have pacemakers or implantable cardiac defibrillators and monitoring these devices during the surgical procedure is critical to ensuring appropriate responses. Atrial fibrillation is also more common with thoracic surgical procedures.

Pulse Oximetry

Pulse oximetry (SpO_2) is a continuous, noninvasive method of measuring the arterial oxygen saturation (SaO_2) from a processed infrared light signal transmitted through a pulsatile vascular bed (a practical application of the Beer–Lambert law). Plethysmography, the measurement of pulsatile volume changes that occur in tissue beds, can also be performed by most pulse oximeters and may have future applications in the noninvasive assessment of fluid responsiveness.

The main goal of pulse oximetry in thoracic surgery is to provide immediate warning of hypoxemia mainly during procedures at high-risk for desaturation such as one-lung ventilation (OLV). This allows for prompt treatment to be initiated before irreversible metabolic derangements occur. During OLV significant desaturation ($\text{SpO}_2 < 90\%$) can occur despite high inspired oxygen concentration secondary to obligate shunt (nonventilated lung) and potentially treatable

intrapulmonary shunting (ventilated lung). Oxygenation during OLV (and during other thoracic surgical procedures) is determined by many factors including cardiac output, blood pressure, blood flow through nonventilated lung, ventilation-perfusion matching in ventilated lung, anesthetic effects on hypoxic pulmonary vasoconstriction (HPV), airway mechanics and reactivity, oxygen consumption and preexisting pulmonary disease. In the 1980s, a significant study by Brodsky J, et al. (Anesthesiology 1985;63:212–3) revealed (based on findings from 19 patients undergoing OLV with continuous pulse oximetry monitoring and simultaneous arterial blood gas analysis) that the pulse oximetry measurements were in good agreement with the arterial blood gas analysis. The greatest discrepancy was about $\pm 6\%$ and these authors concluded that the reliability of the pulse oximetry for the detection of changes in oxygenation was sufficient enough that frequent arterial blood gas analysis was not required. However, arterial blood gas analysis will always have a role in the determination of the safety margin before arterial desaturation in terms of the partial pressure of oxygen (PaO_2) measurement. Once the arterial oxygen saturation drops below 90%, the critical “steep portion” on the sigmoid oxy–hemoglobin dissociation curve, further desaturation might be drastic and need prompt evaluation and intervention. Since significant desaturation does not occur until the PaO_2 falls below 60 mmHg, the pulse oximeter (SpO_2) will not detect large changes in PaO_2 . Interestingly enough, the maintenance of normocarbia is not problematic during OLV (described further in the section “Capnography”) while the inevitable intrapulmonary shunt during OLV makes desaturation likely. As most of the oxygen content in arterial blood is based largely on transportation by hemoglobin, when venous admixture occurs (with blood flow from nonventilated lung mixing with the blood flow from ventilated lung), the ability to compensate for this decrease in the oxygen content is limited. The lungs are unable to compensate for this decrease in the arterial oxygen content by increasing blood flow through ventilated lung.

During thoracotomy or thoracoscopy when the patient is placed in the lateral decubitus position, there is potential for rapid changes in SpO_2 from the compression of mediastinal great vessels in addition to intrapulmonary shunting (OLV). The manipulation of lung parenchyma and/or the mediastinum can lead to the development of cardiac arrhythmias that can affect the pulse oximetry readings as well. The use of electrocautery will also, occasionally, interfere with pulse oximetry.

Judicious perioperative fluid management is of crucial importance for thoracic surgical patients. Respiratory variations in invasive arterial pressure recordings (discussed later) such as systolic pressure variation (SPV) or pulse pressure variation (PPV) are sensitive and specific indicators of fluid responsiveness. There is growing interest in the use of variations in the pulse oximeter plethysmographic waveform amplitude as a noninvasive method of estimating fluid responsiveness. Such ventilatory variations in plethysmographic amplitude can be sensitive to changes in preload and can predict fluid

responsiveness in mechanically-ventilated patients [9]. The “Pleth Variability Index” (PVI, Masimo Corp., Irvine, CA) maybe one such dynamic index automatically derived from pulse oximeter waveform analysis, with potential for clinical applications in the assessment of fluid responsiveness and in monitoring response to therapy. Studies showing that patients with significant dynamic plethysmographic variation will respond to a fluid bolus have been published [7]. However, since different pulse oximeters use different nonstandardized proprietary signal processing plethysmographic algorithms, measurements obtained by one specific device or method may not be applicable to similar variables from other manufacturers [10]. There are several factors other than volume status that can affect plethysmography such as local temperature, site of measurement, influence of venous pressures, etc. [11]. The future application of this plethysmographic aspect of pulse oximetry is ripe for further investigation both during and after thoracic surgery.

Capnography

Monitoring the adequacy of ventilation via CO_2 waveform analysis is usually performed continuously during thoracic surgery by infrared dispersion spectrophotometry or mass spectrometry. Patients undergoing thoracic surgery usually have significant underlying lung disease and a chronic history of smoking, so it is extremely important to recognize the different phases of the time capnograph to recognize the underlying pulmonary pathology (such as obstructive patterns of expiration) as well as distinguish artifacts and errors. The typical CO_2 vs. time waveform (time capnography) is displayed on most anesthesia monitors and has characteristic intervals that represent different physiologic events during ventilation (see Fig. 19.1).

Phase I is the expiratory baseline and represents the exhalation of CO_2 -free gas from anatomic dead space. Phase II is the expiratory upstroke or fast rise phase representing the mixing of dead space gas with alveolar gas containing CO_2 . Phase III

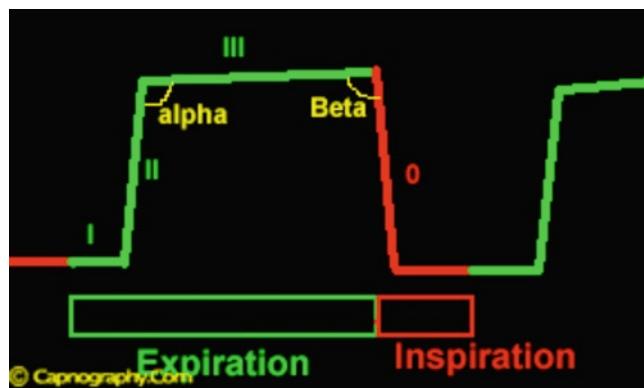


FIG. 19.1. Time capnograph (from Bhavani Shankar Kodali MD. <http://www.capnography.com>. Accessed 10 Feb 2010).

or the alveolar expiratory plateau phase represents the exhalation of CO_2 -rich gas from the gas-exchanging alveoli. The angle between phases II and III has been referred to as the α angle and is an indirect indication of ventilation–perfusion (V/Q) matching. Finally, phase 0 is the inspiratory down-slope during which time fresh gases are inhaled. The nearly 90° angle between phases III and 0 has been referred to as the β angle [12]. This β angle may increase during rebreathing. During thoracic surgery these phases are affected by cardiopulmonary conditions that need to be recognized by the anesthesiologist. A decrease in the slope of phase II may be seen in certain acute and chronic conditions that negatively impact expiratory flow (such as bronchospasm or COPD). This reduction in the slope is determined by the extent of mixing of parallel and series dead space gases with ideally well-mixed alveolar gas. An increase in the α angle appears as a prominent up-sloping in phase III and signifies worsening V/Q matching. This may be due to changes in cardiac output, CO_2 production, airway resistance, and/or functional residual capacity.

In the lateral decubitus position, there are physiologic changes in ventilation and perfusion for both the dependent and nondependent lungs. Phase III of the capnograph has a characteristic biphasic appearance of the waveform. This is believed to occur because the nondependent lung will obtain significantly more ventilation relative to perfusion (high V/Q units) and will contain more alveolar dead space contributing to the earlier and lower part of an up-sloping phase III. The dependent lung will receive more perfusion relative to ventilation (lower V/Q units) and less alveolar dead space consequently contributing to the later and higher part of the phase III plateau. During cross-field ventilation for procedures involving resection of main stem or tracheal masses that require jet ventilation or intermittent apnea, close monitoring and vigilance of the capnogram is pivotal because complete absence of a waveform implies no ventilation, no circulation, or a disconnected capnometer. The end-tidal CO_2 to arterial CO_2 gradient (PaCO_2 – PETCO_2) is related to the extent of dead space ventilation and tends to increase during OLV. Despite occasionally significant oxygen desaturation, the maintenance of adequate ventilation or normocarbia during OLV is usually not problematic.

There is increasing acknowledgement of the similarities between Adult Respiratory Distress Syndrome (ARDS) and OLV [13]. Ventilation strategies originally developed for ARDS may have benefits during OLV. Permissive moderate hypercarbia is becoming a routine component of OLV management and capnography (with intermittent arterial blood gas analysis), will aid in monitoring this approach to ventilation. Increasing minute ventilation to the dependent ventilated lung during OLV in the lateral position removes sufficient CO_2 to compensate for the higher CO_2 content of the pulmonary blood flow perfusing the nonventilated lung. Capnography also enables the detection of improperly-placed double-lumen tubes (DLT) if the tracheal and bronchial lumens are separately and continuously monitored during tube positioning.

Intraoperative Spirometry

With the availability of real-time intraoperative spirometry in the current generation of anesthesia machines, it has become possible to continuously monitor inspiratory and expiratory volumes, pressures, and flows. During thoracic anesthesia, especially with OLV in the patient with preexisting pulmonary disease or at-risk for postoperative complications, breath-by-breath spirometry can guide the early detection of a mal-positioned DLT and help minimize the potential for lung injury by guiding the optimization of ventilatory settings that are individualized to each patient [14].

With the loss of lung isolation, such as with cephalad migration of the DLT, the expired volume will, acutely, decrease significantly to well below the inspired volume (beyond the usual normal 20–30 mL/breath difference that results from the uptake of inspired oxygen) [14]. Similarly, unintentional caudad migration of the DLT can result in a readily apparent decrease in compliance as set tidal volume/pressure is delivered to a single lobe rather than the appropriate lung. The pressure–volume and flow–volume graphs can show characteristic changes. Additional uses for intraoperative spirometry include the identification of auto-PEEP (persistent end-expiratory flow) during OLV, which can be seen on the flow–volume loop. Intraoperative spirometry data (e.g., monitoring compliance and plateau pressures) can be combined with data from arterial blood gases, capnography, and oximetry to make adjustments to ventilatory parameters to optimize gas exchange [14]. The ability to accurately measure differences in inspiratory and expiratory tidal volumes can also be extremely useful to aid in the assessment and management of pulmonary air leaks during pulmonary resections.

Arterial Blood Pressure Monitoring

Given the potential for cardiovascular instability during intrathoracic procedures, the possible need for repeated blood gas analysis, and a patient population with significant underlying comorbidities, the use of invasive arterial blood pressure monitoring is common in current clinical thoracic anesthesia practice to assess beat-to-beat blood pressure and derived functional hemodynamics. Mean arterial pressure (MAP) is the most useful parameter to approximate organ perfusion pressure in noncardiac tissues provided venous or surrounding tissue pressures are not elevated [15].

Technical aspects of the invasive measurement of vascular pressures: The principles described here apply to the invasive measurement of vascular pressures (arterial blood pressure, central venous pressure (CVP) or PAC pressures). The monitoring system typically used in current clinical practice consists of a catheter connected via saline-filled, low-compliance tubing to an electronic transducer. Signal transduction, performed by these so-called dynamic pressure transducers, involves changing either electric resistance or capacitance in

response to changes in pressure on a solid-state device (Wheatstone bridge system) [16]. Pressure waves recorded through intravascular catheters should be transmitted undistorted to the transducer, processed and then displayed. Unfortunately, there are phenomena that can interfere with the accuracy of such systems. Distortion can result from either resonance or damping and produce erroneous readings that need to be recognized. The “fast flush test” is a clinically useful method that allows for the detection of these errors. Readers are directed to comprehensive technical reviews on this topic for further information [16, 17].

Digital numeric readouts of systolic and diastolic pressures that are displayed on the monitors are the running average of values over a certain time interval. From a clinically relevant perspective, the transducer must be placed in the appropriate position relative to the patient. Correct positioning of the pressure transducer is crucial and often most prone to error. Generally, pressures are referenced against ambient atmospheric pressure by exposing the pressure transducer system to air through an open stopcock and pressing the zero-pressure button on the monitor display. The transducer must be horizontally aligned with a specific position on the patient’s body that represents the upper fluid level in the chamber or vessel from which pressure is to be measured [17]. Proper positioning of the pressure transducer is especially critical for measurement of venous pressures (CVP, PAOP) because seemingly small errors in transducer height relative to the patient are amplified. Ideally, transducers should be positioned approximately 5 cm posterior to the left sternal border at the fourth intercostals space, since this point better represents the upper fluid level of the right atrium. This is especially relevant during thoracic surgery when patients are in a lateral position where errors in zeroing/referencing can easily influence therapy. For instance, in the lateral decubitus position, invasive arterial pressure recorded directly from either the right or left radial arteries will remain unchanged relative to the supine position as long as the respective pressure transducers remain at heart level. However, noninvasively measured blood pressure will be higher in the dependent arm and lower in the nondependent arm. Such differences in noninvasive blood pressure measurement are determined by the positions of the arms above and below the level of the heart and are equal to the hydrostatic pressure differences between the level of the heart and the respective arm. Blood pressure is directly related to the cardiac output (CO) and systemic vascular resistance (SVR). This is the hemodynamic corollary to Ohm’s law where electricity (flow or Q) is directly proportional to the voltage (driving pressure gradient across vascular beds or MAP–CVP) and is inversely proportional to resistance (SVR). Adapted to circulation this proportionality can be described as Flow or $Q = (MAP - CVP)/SVR$. While a normal blood pressure does not necessarily reflect hemodynamic stability, hypotension does represent a potential threat to adequate tissue perfusion.

As the arterial waveform is transmitted from the aortic root to the periphery, the actual pressure wave itself becomes

distorted. Aging, hypertension, and atherosclerosis all relatively common in thoracic surgical patients can also influence the displayed arterial waveform. In the peripheral arterial tree, the high-frequency components (such as the dicrotic notch) disappear, the diastolic trough decreases, the systolic peak increases, and there is a transmission delay because there is decreased arterial elastance. Thus, invasive pressure waveform morphology and actual pressure values depend on the site of pressure measurement. Pulse contour analysis-based devices are, therefore, susceptible to mechanical errors in arterial pressure measurement and to such distal pulse amplification. Consequently, clinical therapy is often better-guided using mean arterial pressure than systolic or diastolic blood pressure measurements. The use of arterial pressure-derived variables such as SPV, PPV, deltaDown, etc., are discussed below under non-invasive hemodynamic monitoring.

Central Venous Pressure

Technical aspects of invasive pressure measurement are described in the previous section. CVP represents the back pressure to systemic venous return and is, in effect, an estimate of right ventricular filling pressure. An appropriately inserted central venous catheter is required for actual CVP measurement and placing a catheter on the same side as the thoracic operation (internal jugular or subclavian) allows for an unintentional pneumothorax to be treated by the pleural drainage tube that is usually inserted for most thoracic surgical procedures. Routine placement of central venous catheters are not justified but the risks may be worth taking if it is likely that infusions of vasoactive drugs will be used, blood products may need to be rapidly administered, or when large-bore peripheral venous access is not obtainable.

CVP might be inaccurate after the establishment of a pneumothorax during thoracic surgery, during the resection of mediastinal masses compressing the right heart chambers, and also during lateral positioning or with an open chest. Tumors invading cardiac structures can also produce erroneous CVP values. The use of isolated CVP measures to guide fluid therapy during thoracic procedures is not desirable given the evidence against the use of static hemodynamic measures. Changes in CVP over time are more clinically relevant than absolute numeric values. There are no clear CVP “cut-offs” that can reliably distinguish between patients whose cardiac output will and will not change in response to a fluid bolus [18, 19]. A volume-responsive patient is better identified by, and fluid therapy is better titrated using dynamic or functional hemodynamic indices (see Fig. 19.2). There are several factors that can make venous pressure measurement a poor surrogate for the determination of intravascular volume status. The cardiac pressure–volume relationships are non-linear. Ventricular compliance may change intraoperatively and dynamically based on the effects of anesthesia, drugs, and ongoing pathophysiology. Such changes in compliance

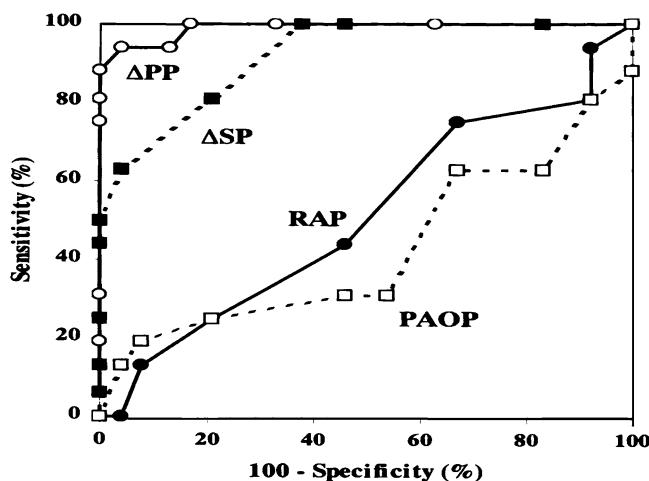


FIG. 19.2. Receiver operating curve (ROC) for right atrial pressure (RAP), Pulmonary artery occlusion pressure (PAOP), delta systolic pressure (Δ SP) and delta pulse pressure (Δ PP) to predict a response to volume challenge. Only the dynamic parameters allow prediction beforehand if the patient will improve cardiac performance in response to a volume challenge. Using a cut-off value of 13% for Δ PP allows almost perfect prediction of which patients respond to a volume challenge (area under the ROC curve of 90%). Static parameters (CVP, PAOP) are no better than a coin toss with area under the ROC curve of approximately 50%.

produce changes in CVP without any significant changes in volume status. In addition, the physiologically-relevant determinant of ventricular preload is the transmural pressure (the difference between intracardiac and intrathoracic-extracardiac pressure) [18] and not the CVP (which is referenced against the atmospheric pressure).

Positive end-expiratory pressure (PEEP) and variable intrathoracic pressures, which can both be seen during thoracic procedures, can influence preload by affecting transmural pressures. For instance, higher levels of PEEP necessary to maintain oxygenation may *raise* the CVP while *reducing* venous return. When viewed in isolation, such a CVP measure does not reflect this paradoxical effect [19]. Occasionally, the CVP waveform morphology can also provide clues to diagnosis and management [16]. Examples include the absence of the “a” wave in atrial fibrillation, cannon “a” waves during junctional rhythm, and a combined “cv” wave with an absent \times descent in moderate–severe tricuspid regurgitation. The displayed digital value for CVP is influenced by such tall regurgitant waves and does not necessarily reflect the right ventricular preload.

Pulmonary Artery Catheter Monitoring

The balloon-tipped flow-directed Pulmonary Artery Catheter (PAC) can provide an estimate of cardiac output, accurate measurement of right atrial and right ventricular pressures, pulmonary arterial pressures, and an estimate of left ventricular filling pressures (via measurement of the pulmonary artery occlusion pressure). Clinically relevant technical aspects of

invasive pressure measurement are described in the previous section. Use of pulmonary artery diastolic pressures or pulmonary artery occlusion pressures as an estimate of left ventricular preload is subject to many confounding factors, including dynamic changes in ventricular compliance and juxtagardiac transmural influences. Both under- and overestimation of the left ventricular end-diastolic volumes are possible with the PAC. Variable intrathoracic pressures and PEEP during thoracic surgery can have an adverse influence on PAC-based pressure measurements. Practically, the use of the PAC has been largely limited in present-day thoracic anesthesia. Hemodynamic therapies guided by specific PAC-derived pressure “cut-off” values do not result in systematically better results. In the large rigorous RCT by Sandham et al. [4], patients with PACs did not accrue any significant improvements in outcome vs. standard care during high-risk surgery (including thoracic surgical patients). Further, the FACTT study showed that PAC-guided therapy in ARDS and Acute Lung Injury did not improve survival relative to CVC-guided therapy [20]. This lack of benefit further discourages the use of the PAC as a monitor to guide fluid therapy for the thoracic surgical patient who is at-risk for developing ARDS/ALI [20]. Other problems with PACs also include the significant potential for data misinterpretation, risks for mechanical complications like arrhythmias, pulmonary infarction, pulmonary artery rupture, thromboembolism, infectious risks, and potential for cardiac valvular/endocardial injury.

The PAC is still occasionally indicated when the accurate measurement of cardiac output is of critical importance or in the setting of severe pulmonary hypertension or right ventricular dysfunction. The air-filled PAC balloon tends to float to nondependent regions as it passes into the pulmonary vasculature. During thoracic surgery appropriate positioning of the PAC in the lateral position during lung isolation is a challenge since most of the perfusion is largely directed by HPV to the dependent lung. So for accurate estimation of cardiac output, the PAC will need to be “floated” into the correct pulmonary artery prior to surgical positioning. Thermodilution-based cardiac output monitoring, the most widely used clinical technique, is subject to measurement errors introduced by rapid intravenous fluid administration, tricuspid valve regurgitation, and may be unreliable during OLV. “Oximetric” PACs can measure mixed venous hemoglobin oxygen saturation and continuously display a Fick-principle based cardiac output. Mixed venous hemoglobin desaturation is a reflection of the global inadequacy of cardiac output relative to global oxygen requirements, and is also influenced by arterial hemoglobin oxygen desaturation and a reduction in the overall hemoglobin content. “Volumetric” PACs use a rapid-response thermistor, and by measuring residual thermal signal, can be used to estimate the right-ventricular end-diastolic volume (RVEDV). Such PACs can be used to monitor RVEDV and may indicate right-heart failure if the RVEDV increases as cardiac output decreases – such as may be seen in patients with cor pulmonale presenting for thoracic surgery. Pathophysiologic conditions involving left-sided cardiac structures (mitral valvular disease,

LV dysfunction) can also produce characteristic changes in the PAC waveforms.

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) is a powerful technology that has become a routine monitor in the operating room for cardiac surgery and for some specific thoracic surgeries. It provides instantaneous and continuous assessment of cardiac function and structure. The only absolute contraindication to the insertion of the TEE probe during thoracic surgery is a planned esophageal surgery. There are several relative contraindications such as esophageal varices, strictures, severe esophagitis, Zencker's diverticulum, following recent heparinization, Scleroderma, undiagnosed dysphagia, and patients with a history of chest radiation therapy.

Multiple studies have also documented the improved sensitivity of the TEE for the detection of myocardial ischemia relative to ECG-based automated ST-segment monitoring or PAC measurements. The presence of regional wall motion abnormalities (RWMA) on TEE is a sensitive sign of myocardial ischemia. The earliest sign of ischemia is impaired ventricular relaxation (impaired lusitropism) followed by impaired contractility (impaired inotropism), then impaired global systolic function, followed by changes in ventricular pressure–volume relationship, and one of the last signs is the development of ST-segment changes on the ECG. In addition, the TEE may be inserted in intubated, hemodynamically unstable patients for prompt identification of the etiology of shock and to monitor response to interventions such as fluid-loading, vasopressor, or inotrope infusions. Other applications of the TEE in thoracic surgery are for the evaluation of pericardial tamponade, pleural effusions, identification of intracardiac lesions responsible for hypoxemia (right-to-left shunts), and for the evaluation of the cardiac function during pneumonectomy. Some quantitative tools such as color-flow mapping (CFM) and Doppler echocardiography have further enhanced the role of TEE in thoracic surgery. CFM allows for the evaluation of congenital cardiac lesion and vascular malformations. Doppler echocardiography enables accurate assessment of valvular pathology and flow-based measurement. Tissue Doppler imaging enables the assessment of diastolic dysfunction. Recently, the role of TEE in thoracic oncologic surgery has been so important that now this technology has expanded to include the staging of locally advanced lung cancers [21], such as in the setting of patients with locally advanced nonsmall cell lung cancer with suspected involvement of cardiac structures and/or great vessels. TEE technology can also be applied to evaluate the resectability of certain lung cancers especially when CT-imaging is suspicious for local invasion thus unnecessary futile thoracotomy can be avoided.

Although time-consuming quantitative measurements of left ventricular performance and filling can be made, with appropriate training, anesthesiologists can use the TEE to readily distinguish between hypovolemic, cardiogenic, and

obstructive causes of hemodynamic collapse. The assessment of valvular structure and function, especially in patients with preexisting aortic and mitral defects presenting for thoracic surgery, is readily made with a comprehensive TEE examination. A recent study concluded that TEE measured IVCD at the atrio-caval junction showed statistically significant correlation with the mean CVP [22]. Almost one-third of all patients with signs and symptoms of congestive heart failure will have preserved systolic function but diastolic dysfunction. The diagnosis of impaired diastolic relaxation or restricted filling is currently made by echocardiography and is not easily accessible by other monitoring tools. In both endovascular and open surgical procedures involving the thoracic aorta, the TEE has a critical intraoperative role to play.

Minimally- and Noninvasive Hemodynamic Monitoring Devices and Tissue Perfusion Monitoring

As in other intraoperative situations, in the thoracic surgical patient, the goal of hemodynamic monitoring is to identify threats to adequate tissue perfusion early, to intervene using goal-directed therapy, and to track response to such therapy. The rational use of fluids is critical, in thoracic surgical patients, given the recognition that traditional approaches to fluid therapy may result in less optimal outcomes [23–27]. For instance, fluid restriction in pulmonary resection surgery is a well-recognized approach to management with proven benefits [28]. When compared with conventional intraoperative assessment (physical examination, fluid input and output measurements, etc.), fluid administration guided by flow monitoring can improve outcomes [26]. Furthermore, there is evidence that compared to catheter-based measurements (such as cardiac output by thermodilution or CVP), therapeutic management based on certain less-invasive cardiac output monitors leads to fewer complications and shorter length of stay [24–26]. The dangers of inadequate cardiac output secondary to hypovolemia need to be balanced against the dangers of fluid overloading in these patients. Increasingly, dynamic indices of fluid responsiveness are being monitored to guide intraoperative fluid therapy [29, 30]. Functional hemodynamic monitoring is a term often used to describe the use of monitoring to evaluate treatment efficacy. The devices described below are minimally- or noninvasive when compared with central venous catheters, PACs and TEE. Table 19.1 provides a comparison of the different minimally-invasive monitoring technologies.

Key functional hemodynamic questions applied to thoracic surgical patients include: is flow (cardiac output) adequate to meet global tissue demands, will flow increase with fluid loading, and is hypotension a reflection of reduced flow or vascular tone or both. Therapies are consequently based on the identification of the potential for tissue hypoperfusion and the likelihood that fluid loading alone (preload responsiveness) and/or the use of inotropes or vasopressors will increase

TABLE 19.1. Comparison of currently clinically useful minimally-invasive hemodynamic monitoring devices.

Noninvasive hemodynamic device	Calibration required	Arterial waveform high fidelity	Hemodynamic parameters calculated	Requires central line insertion
FloTrac and Vigileo	No	Yes	SVV, SV, CO, SVR	No
Esophageal Doppler Monitoring (EDM)	No	No	SV, CO, and FTc (flow corrected time)	No
LiDCO (Lithium Dilution Cardiac Output)	Yes (lithium)	Yes	SVV, SV, CO, SVR, DO ₂	Yes
LiDCO Rapid	No	Yes	SVV, SV, CO, SVR	No
PiCCO (Pulse Intermittent Continuous Cardiac Output)	Yes	Yes	SVV, SV, CO, SVR, EVLW, ITTV, CI	Yes

SVV Stoke volume variation; SV stroke volume; SVR systemic vascular resistance; CO/CI cardiac output/index; FTc heart rate corrected flow time; DO₂ oxygen delivery in cc/min; EVLW extra vascular lung water; ITTV intrathoracic thermal volume

flow and mean arterial pressure. The stroke volume, systolic arterial pressure, and pulse pressure all vary in hypovolemic patients during positive pressure ventilation with fixed tidal volumes [31, 32].

Stroke volume variation (SVV), SPV, and PPV measure different but related aspects of cardiorespiratory interaction. These variables have been shown to be superior to the conventional estimates for preload responsiveness such as CVP and PAOP. Figure 19.3 shows the receiver operating curve for SVV and PPV [24–26]. In other words, the ability to increase flow with volume loading is better predicted by the SVV, SPV, and/or PPV especially in patients undergoing surgical procedures with an expected substantial blood loss or fluid-compartment shifts (compare with Fig. 19.2). These variables are directly measured from the arterial pressure tracing and its variation with ventilation. During controlled mechanical ventilation there are respirophasic changes in venous return and consequently subtle changes in pulse pressure and systolic pressure with each respiratory cycle. Figures 19.4 and 19.5 graphically display the physiologic mechanisms underlying these observations.

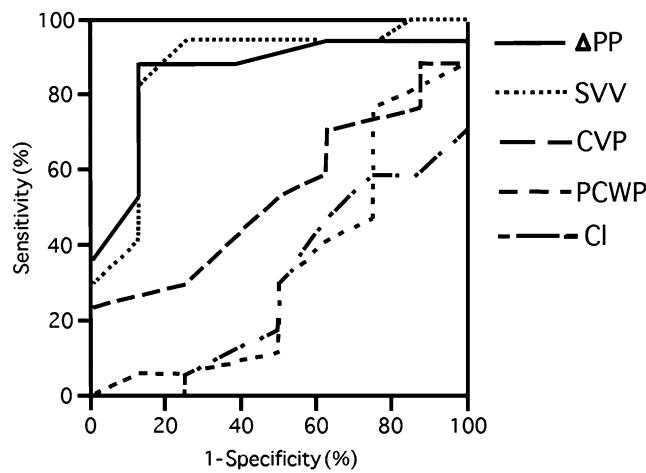


FIG. 19.3. Only the dynamic variables Δ PP and SVV allow discrimination of responders from non-responders to a volume challenge. Add also – CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac input.

Esophageal Doppler Monitoring

Esophageal Doppler Monitoring (EDM) was first introduced in 1975. Since that time it has been the most common minimally-invasive hemodynamic monitor used and studied for individualized hemodynamic optimization and goal-directed therapy in thoracic surgery. Based on the Doppler principle, the probe which is inserted into the mid-esophagus transmits a continuous wave Doppler signal aligned with flow in the descending thoracic aorta at the tip of the device. The ultrasound beam is directed as parallel to the pathway of the red blood cells (traveling through the descending thoracic aorta) as possible. The constant motion of the red blood cells reflects a fraction of these ultrasound signals. The relative shift in the frequency of returned signals is called the Doppler shift and this shift is proportional to the peak red blood cell velocity. The displayed velocity vs. time profile allows the hemodynamic calculation of stroke volume and cardiac output (based on certain assumptions). This device allows immediate real-time, comprehensive left ventricular flow-based assessment of the effects of changes in preload, afterload, contractility, and rhythm and on stroke volume. This device has been validated against the thermodilution PAC.

The caveat with this device is that it *estimates* the cross-sectional area of the descending thoracic aorta based on patients' demographics from a nomogram including age, height, and weight. Also, the angle between the direction of blood flow in the descending thoracic aorta and the Doppler signal sent by the esophageal probe is greater than the ideal 20° angle, so flow can be underestimated (although automated corrections are made for this difference). Furthermore, assumptions on the ratio of blood flow distribution to the upper vs. the lower body are also made. These correction factors can generate inaccuracies when exposed to interventions that affect blood flow distribution such as when using thoracic epidural analgesia. The esophageal Doppler device is very sensitive to positioning for the probe, leading to a need for frequent repositioning when trying to obtain accurate data. The use of electrocautery also interferes with data acquisition. The technology also allows for the calculation of Flow Time corrected for heart rate (FTc). This is the time that it takes for the left ventricle to eject the stroke volume or

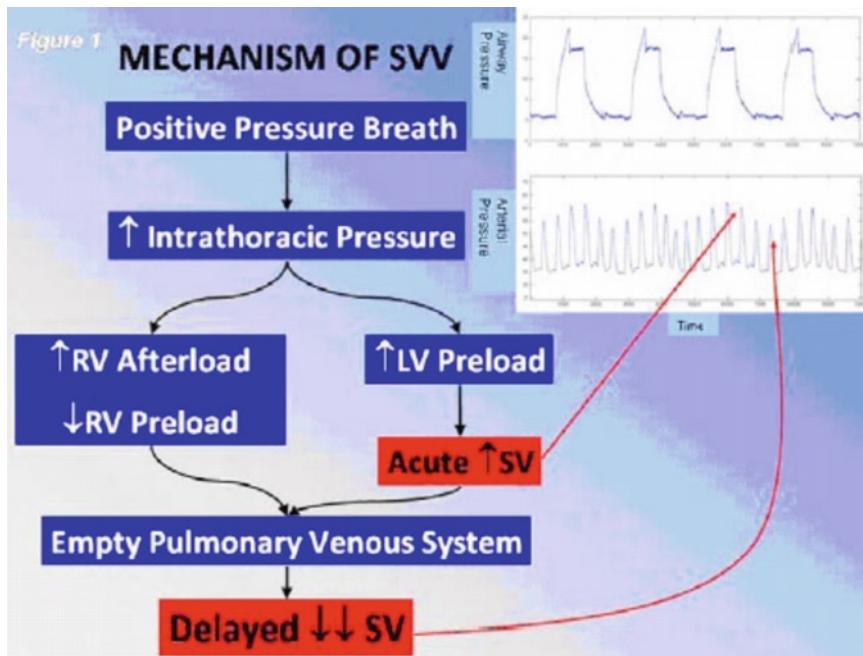


FIG. 19.4. Results in an acute increase in LC SV coincident with the inspiratory phase of positive pressure ventilation.

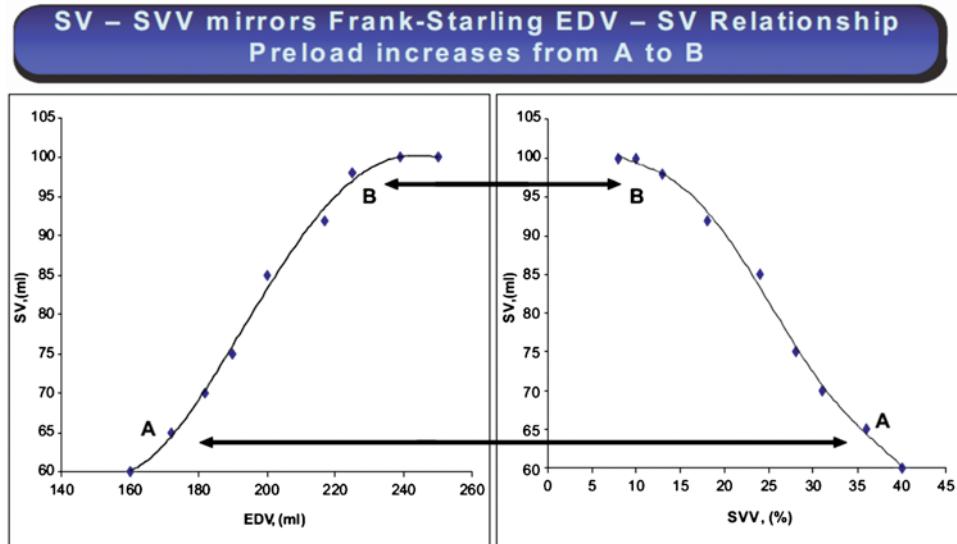


FIG. 19.5. Simultaneously developed Frank-Starling curve with the corresponding SV-SVV relationship in an individual patient undergoing volume resuscitation. The SV-SVV relationship mirrors the Frank-Starling curve: as preload increased, cardiac performance reaches a plateau similarly declining SVV is associated with improved cardiac performance. SVV-SV pairs can provide information about cardiac performance similar to a Frank-Starling curve. EDV end diastolic volume.

the systolic flow time in the descending thoracic aorta corrected for heart rate. The typical range for the FTc is 330–360 ms. The more volume loaded the ventricle is, the longer it takes to eject the stroke volume, conversely the more volume depleted the ventricle is, the lesser time it takes to eject the stroke volume. The FTc usually decreases to under 300 ms in volume-depleted patients. The FTc has been used in algorithms for goal-directed fluid therapy [33], however it remains a function of contractility, preload and SVR and as such vascular impedance significantly

affects this variable. In thoracic surgical patients, it has been demonstrated that this device can be used to detect and correct low-flow conditions and to guide hemodynamic support during the intraoperative period [33, 34].

Unfortunately, the EDM cannot be used during esophageal procedures where fluid management is pivotal to length of hospital stay and outcomes. The goals during these often lengthy procedures (such as esophagectomy for esophageal cancer) are to be more liberal with fluids during the abdominal

portion of the surgery and more conservative during the thoracic portion of the procedure.

Continuous Pulse Contour Analysis (PiCCO)

This device estimates cardiac output using a combination of transpulmonary thermodilution and arterial contour waveform analysis. Both the thermal indicator and the pressure waveform must be measured simultaneously from a central line and an arterial line (either femoral or axillary) for calibration. This is impractical in the operating room setting and consequently this technology is largely limited to use in Europe in the Intensive Care Unit setting. Stroke volume is estimated from the portion of the arterial waveform that corresponds to systole. The pulsatile systolic pressure-time integral (multiplied by the heart rate to give an estimated cardiac output) is calibrated against the transpulmonary thermodilution technique of cardiac output measurement. The advantage of calibration against transpulmonary thermodilution is its independence relative to the influence of ventilation and the respiratory cycle. PiCCO has also been validated against continuous cardiac output monitoring offered by the PAC. This technology relies on a high fidelity arterial waveform and is, therefore, sensitive to damping and resonance where errors in the estimation of the cardiac output may occur. Another limitation of the PiCCO system is that conditions that interfere with the calibration process or pulse contour waveform analysis such as intracardiac shunts, severe aortic valvular disease, and the use of intraaortic balloon pump devices introduce errors [35]. As of the time that this section was written, there have been no prospective randomized controlled outcome studies published in thoracic surgery using the PiCCO system as part of goal-directed therapy (GDT).

Lithium Dilution Cardiac Output

This technology is based on the physics of pulse power analysis, which is independent of the waveform morphology, and has a correction factor incorporated to account for impedance and arterial compliance. Based on an understanding that pulse pressure measured from the arterial trace is a combination of an incident pressure wave ejected from the aorta and a reflected wave from the periphery, stroke volume calculation requires that the two waves need to be separated. The algorithm takes into consideration the fact that the arterial pressure wave changes in size depending upon the proximity of the sampling site to the heart and also on patient's age. The use of an indicator dilution method for calibration (in this case lithium since it does not naturally occur in plasma and therefore can generate a high signal-to-noise ratio) allows the measurement of blood flow, with a lithium ion-selective electrode situated in an arterial line sensing the extent of dilution. These data

are used to generate a concentration vs. time curve and the cardiac output can then be calculated from the known amount of lithium and the area under the concentration-time curve (standard indicator-dilution technique for cardiac output estimation). Multiple studies have compared continuous cardiac output measurement via PACs with the Lithium Dilution Cardiac Output (LiDCO plus) system and have found acceptable correlation (defined as agreement of measured values within 15% of each other). There have been multiple studies confirming that lithium dilution is comparable to intrapulmonary thermodilution over a range of cardiac outputs. This is very important in thoracic surgical patients with poor ventricular function and in individual patients with a fluctuating cardiac output or with a hyperdynamic circulation [36].

This device has to be calibrated because the proprietary algorithm lacks the ability to independently assess the effects of constantly changing vascular tone on stroke volume measurement. Another limitation of this technology revolves around the use of lithium. Nondepolarizing muscle relaxants cross-react with the lithium sensor and can cause the sensor to drift. Calibration may also be unreliable in patients with severe hyponatremia. For intraoperative use, calibration needs to be performed either before induction or after the initial hemodynamic stress from airway management has had time to subside. The device can be onerous for the operating room and it is currently mainly used in the ICU setting. The accuracy of the device is compromised in patients with severe peripheral vascular or aortic valve disease and in those requiring intraaortic balloon counter pulsation therapy. A high fidelity arterial waveform is mandatory for accurate hemodynamic data.

The LiDCO Rapid is a recently introduced alternative designed for the operating room setting. This technology uses the same internal algorithm as the LiDCO plus but allows for the calculation of other hemodynamic parameters. The device analyses the arterial pressure waveform and using the pulse power cardiac output algorithm converts pulse pressure into a nominal stroke volume and cardiac output. The device does not require calibration with lithium and uses a nomogram for calculation of arterial compliance. There are no published studies at the time of this review that examine the use of this technology during thoracic surgery.

Arterial Pressure Cardiac Output Device (APCO, FloTrac/Vigileo)

This technology is based on the physical principle of the relationship between pulse pressure and stroke volume. Arterial pulse pressure is directly proportional to left ventricular stroke volume and is inversely related to aortic compliance. Once stroke volume is determined by the internal algorithm, the pulse rate is counted and cardiac output is estimated. The device does not require external calibration because the algorithm, in theory, corrects and compensates for dynamic changes in vascular tone. The device calculates cardiac output

on a continuous basis (in a 20-s averaging cycle or a 5-min averaging cycle) [37–41]. With the FloTrac/Vigileo device, the arterial pressure waveform morphology is used to analyze the pulse rate and examine the variation (skewness, kurtosis, and standard deviation) of the waveform to determine changes in stroke volume. Finally, the device takes into account the multiple variables responsible for the changes in vasculature compliance (a so-called Ki factor). This constant is derived from the patient's specific vascular compliance based on biometric values (age, height, sex, and weight). The second-generation software tended to underestimate the cardiac output when the SVR was less than 800 dynes such as in sepsis and during liver transplants secondary to the hyperdynamic state typical of these situations. With the development of the third-generation software, the estimation of the cardiac output is more accurate and newer data have demonstrated clinically acceptable precision in hyperdynamic states. Presumably, this will lead to further important studies in the near future in thoracic surgical patients. The accuracy of the device is compromised in patients with severe peripheral vascular or aortic valvular disease and in those requiring intraaortic balloon counter pulsation therapy. A high fidelity arterial line waveform is mandatory for accurate hemodynamic data. The technology has been studied during cardiac surgery and in the postoperative cardiac surgical population. Precision and bias in the estimation of cardiac output (using Bland–Altman analyses) are acceptable relative to the gold-standard thermodilution PAC measurement [39–41]. Data relevant to thoracic surgical patients are sparse.

In addition, central venous oximetry can be integrated into decision making with this device. This technology allows for the measurement of the superior vena cava oxygen saturation ($SvcO_2$) via insertion of an 8 Fr fiber-optic double-lumen catheter into the jugular or subclavian veins (using the same physical principle of spectrophotometry used for pulse oximetry). The measured value is 5–7% higher than the true mixed venous oximetry since only the upper extremities, neck and head venous effluent is captured. With PACs, mixed venous oximetry can be performed and coronary sinus and lower extremities effluent causes the measured value to be lower (global mixed venous effluent saturation is measured rather than central venous saturation). Despite the fact that the difference in saturation is 5–7% higher with the $SvcO_2$ than with SvO_2 , it is still a very good surrogate and may be used as a sensitive marker for GDT in high-risk surgical patients undergoing elective thoracic surgery.

References

1. Wendon J. Cost effectiveness of monitoring techniques. In: Pinsky MR, Payen D, editors. Functional hemodynamic monitoring. 1st ed. New York: Springer; 2005.
2. Grocott MPW, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcomes in adults. *Anesth Analg*. 2005;100:1093–106.
3. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345:1368–77.
4. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med*. 2003;348:5–14.
5. Kaplan J, Slinger P, editors. Thoracic anesthesia. 3rd ed. Philadelphia: Churchill Livingstone; 2006.
6. Schroeder RA, Barbeito A, Bar-Yosef S, Mark JB. Cardiovascular monitoring. In: Miller R, Eriksson L, Fleisher L, Wiener-Kronish J, Young W, editors. Miller's anesthesia. 7th ed. Philadelphia: Churchill Livingstone; 2010. p. 1267–328.
7. Landesberg G, Mosseri M, Wolf Y, Vesselov Y, Weissman C. Perioperative myocardial ischemia and infarction. Identification by continuous 12-lead electrocardiogram with online ST-segment monitoring. *Anesthesiology*. 2002;96:264–70.
8. Sgarbossa EB, Pinski SL, Barbagelata A, et al. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. *N Engl J Med*. 1996;334:481–7.
9. Cannesson M, Delannoy B, Morand A, et al. Does the Pleth variability index indicate the respiratory-induced variation in the plethysmogram and arterial pressure waveforms? *Anesth Analg*. 2008;106(4):1189–94.
10. Natalini G, Rosano A, Taranto M, et al. Arterial versus plethysmographic dynamic indices to test responsiveness for testing fluid administration in hypotensive patients: a clinical trial. *Anesth Analg*. 2006;103(6):1478–84.
11. Perel A. Automated assessment of fluid responsiveness in mechanically ventilated patients. *Anesth Analg*. 2008;106(4):1031–3.
12. Components of a time capnogram. http://www.capnography.com/new/index.php?option=com_content&view=article&id=72&Itemid=95. Accessed 10 Feb 2010.
13. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin*. 2008;26:241–72.
14. Van Limmen JGM, Szegedi LL. Peri-operative spirometry: tool or gadget? *Acta Anaesthesiol Belg*. 2008;59:273–82.
15. Pinsky MR, Payen D. Functional hemodynamic monitoring. *Crit Care*. 2005;9:566–72.
16. Barbeito A, Mark JB. Arterial and central venous pressure monitoring. *Anesthesiol Clin*. 2006;24:717–35.
17. Courtois M, Fattal PG, Kovacs Jr SJ, et al. Anatomically and physiologically based reference level for measurement of intracardiac pressures. *Circulation*. 1995;92(7):1994–2000.
18. Magder S, Georgiadis G, Cheong T. Respiratory variations in right atrial pressure predict the response to fluid challenge. *J Crit Care*. 1992;7:76–85.
19. Marik P, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest*. 2008;134:172–8.
20. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med*. 2006;354:2213–24.
21. Caterino U, Dialetto G, Covino FE, et al. The usefulness of transesophageal echocardiography in the staging of locally advanced lung cancer. *Monaldi Arch Chest Dis*. 2007;67(1):39–42.
22. Arthur ME, Landolfo C, Wade M, Castresana MR. Inferior vena cava diameter (IVCD) measured with transesophageal echocardiography (TEE) can be used to derive the central venous pressure (CVP) in anesthetized mechanically ventilated patients. *Echocardiography*. 2009;26(2):140–9.

23. Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: a critical analysis of the evidence. *Chest*. 2002;121:2000–8.
24. Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology*. 2002;97(4):820–6.
25. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds M, Bennett D. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomized, controlled trial. *Crit Care*. 2005;9:R687–93.
26. Donati A, Loggi S, Preiser J, Orsetti G, et al. Goal-directed intraoperative therapy reduces morbidity and length of hospital stay in high-risk surgical patients. *Chest*. 2007;132:1817–24.
27. Venn R, Steele A, Richardson P, et al. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth*. 2002;88:65–71.
28. Diaper J, Ellenberger C, Villiger Y, et al. Transthoracic Doppler monitoring for fluid and hemodynamic treatment during lung surgery. *J Clin Monit Comput*. 2008;22(5):367–74.
29. Lobo S, Lobo F, Polachini C, Patini D, et al. Prospective, randomized trial comparing fluids and dobutamine optimization of oxygen delivery in high-risk surgical patients. *Crit Care*. 2006;10(R72):1–11.
30. Lobo S, Salgado P, Castillo V, Borim A, et al. Effects of maximizing oxygen delivery on morbidity and mortality in high-risk surgical patients. *Crit Care Med*. 2000;28(10):3396–404.
31. Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology*. 2005;103:419–28.
32. Michard F, Boussat S, Chemla D, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med*. 2000;162:134–8.
33. Phan TD, Ismail H, Heriot AG, et al. Improving perioperative outcomes: fluid optimization with the esophageal Doppler monitor, a metaanalysis and review. *J Am Coll Surg*. 2008;207(6):935–41.
34. Slinger PD, Campos JH. Anesthesia for thoracic surgery. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. *Miller's anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2009.
35. Morgan P, Al-Subaie N, Rhodes A. Minimally invasive cardiac output monitoring. *Curr Opin Crit Care*. 2008;14:322–6.
36. De Waal EC, Wappler F, Wolfgang F. Cardiac output monitoring. *Curr Opin Anesthesiol*. 2009;22:71–7.
37. Manecke GR, Auger WR. Cardiac output determination from the arterial pressure wave: clinical testing of a novel algorithm that does not require calibration. *J Cardiothorac Vasc Anesth*. 2007;21:3–7.
38. Breukers RM, Sepehrkhoy S, Spiegelenberg SR, et al. Cardiac output measured by a new arterial pressure waveform analysis method without calibration compared with thermodilution after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2007;21:632–5.
39. Mayer J, Boldt J, Wolf MW, et al. Cardiac output derived from arterial pressure waveform analysis in patients undergoing cardiac surgery: validity of a second generation device. *Anesth Analg*. 2008;106:867–72.
40. Scheeren TW, Wiesenack C, Compton FD, et al. Performance of a minimally invasive cardiac output monitoring system (Flotrac/Vigileo). *Br J Anaesth*. 2008;101:279–80.
41. Mehta Y, Chand RK, Sawhney R, et al. Cardiac output monitoring: comparison of a new arterial pressure waveform analysis to the bolus thermodilution technique in patients undergoing off-pump coronary artery bypass surgery. *J Cardiothorac Vasc Anesth*. 2008;22:394–9.
42. McGee WT. A simple physiologic algorithm for managing hemodynamics using stroke volume and stroke volume variation. *J Int Care Med*. 2009;24(6):352–360.

Intraoperative Transesophageal Echocardiography for Thoracic Surgery

Massimiliano Meineri

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Abbreviations

TEE	Transesophageal echocardiography
3D TEE	Three-dimensional transesophageal echocardiography
TTE	Transthoracic echocardiography
Anatomy	
LV	Left ventricle
RV	Right ventricle
LA	Left atrium
RA	Right atrium
LVOT	Left ventricular outflow tract
RVOT	Right ventricular outflow tract
PFO	Patent foramen ovale
TV	Tricuspid valve
PV	Pulmonic valve
IAS	Interatrial septum
IVS	Interventricular septum
IVC	Inferior vena cava
SVC	Superior vena cava
PA	Pulmonary artery
RPA	Right pulmonary artery
LPA	Left pulmonary artery
PV	Pulmonary veins
LUPV	Left upper pulmonary vein

LLPV	Left lower pulmonary vein
RUPV	Right upper pulmonary vein
RLPV	Right lower pulmonary vein
TEE views	
TG SAX	Transgastric short axis view
ME 4C	Mid-esophageal four-chamber view
ME 2C	Mid-esophageal two-chamber view
ME RV in-out	Mid-esophageal right ventricle inflow-outflow view
ME BiC	Mid-esophageal bicaval view
ME Asc Ao SAX	Mid-esophageal ascending aorta short axis view
UE Ao Arch SAX	Upper-esophageal aortic arch short axis view
Measures	
LVEDD	Left ventricular end-diastolic diameter
LVESD	Left ventricular end-systolic diameter
LVEDA	Left ventricular end-diastolic diameter
LVESA	Left ventricular end-systolic area
LVEDV	Left ventricular end-diastolic volume
LVESV	Left ventricular end-systolic volume
RVEDA	Right ventricular end-diastolic area
FS	Fractional shortening
FAC	Fractional area change

LVEF	Left ventricular ejection fraction
SV	Stroke volume
TAPSE	Tricuspid valve annular plane systolic excursion
TR	Tricuspid regurgitation
RVSP	Right ventricular systolic pressure

Key Points

- Despite its intuitive advantages, the use of TEE in noncardiac surgery has been limited by the availability of trained anesthesiologists, the cost of the equipment and, ultimately, by the lack of updated guidelines. In fact, very few studies have looked at the impact of intraoperative TEE in noncardiac surgery on patients' outcomes.
- TEE is a considered a safe technique. However, despite its relative noninvasiveness, it carries potentially drastic complications and needs to be supported by congruent indications.
- Basic hemodynamic monitoring can be easily achieved with TEE. Qualitative and quantitative assessments of right and left ventricular function are feasible and can be integrated as a complete standard in intraoperative hemodynamic monitoring.
- TEE for lung transplant is considered a category II indication by current guidelines. TEE provides ideal intraoperative hemodynamic monitoring, and it allows the assessment of all vascular anastomoses immediately after the reperfusion of the graft.
- TEE has a promising role in the diagnosis and follow-up of both acute and chronic pulmonary embolisms. TEE can easily detect and monitor the effects of acute and chronic pressure overload on the right ventricle and can rule out dangerous intracardiac shunts. These characteristics make it a powerful tool for intraoperative monitoring during pulmonary embolectomy and endarterectomy surgeries.
- The ability to image cardiac structures with a high spatial resolution makes TEE suitable for assessing the effect of mediastinal masses on cardiac chambers. TEE may also provide useful information to guide surgical resection.

Introduction

The use of TEE outside of the cardiac operating room has significantly increased over the last few years. Thoracic surgery is naturally becoming an exciting field for the application of this powerful technology for more than one reason. In fact, in many institutions, cardiac anesthetists, many of whom are TEE trained, provide their services to thoracic surgery. Moreover, the physiology of cardiopulmonary interaction, the growing number of combined cardiothoracic operations and the increasing complexity of patients' pathologies create the need for the complete intraoperative monitoring of cardiac function.

The lack of updated guidelines for the use of TEE for intraoperative hemodynamic monitoring of noncardiac surgery

transplant makes its practice around the world very variable. If the use of the pulmonary artery catheter has been accepted as the standard of care, despite the lack of outcome studies, intraoperative use of TEE has not yet found a definite indication despite its obvious advantages [1].

Indications for TEE in Thoracic Surgery

Indications for the use of intraoperative TEE in thoracic surgery can be derived from the current American Society of Anesthesiologists guidelines [2] for perioperative use of TEE. They comprise Category I–III indications. Category I is supported by strong evidence or expert opinion and includes acute or persistent life-threatening intraoperative hemodynamic instability. Category II indications are supported by weaker evidence or expert consensus, and include the monitoring of patients at-risk for hemodynamic instability and myocardial ischemia. The definition of the risk for intraoperative hemodynamic disturbances is multifactorial and is based on the patient characteristics, the type of surgery, and the clinical setting (Table 20.1).

Intraoperative monitoring of patients undergoing pulmonary embolectomy and the assessment of vascular anastomoses in the course of lung transplant are also Category II indications. Category III indications are supported by little scientific or expert support and includes the use of TEE for guiding catheter placement and the intraoperative evaluation of pleuro-pulmonary disease.

By reviewing the most relevant studies on the use of TEE for intraoperative hemodynamic monitoring in noncardiac surgery (Table 20.2), we found that TEE directed changes in the intraoperative hemodynamic management in 27–80% of the patients and in another 1–23% altered the surgical plan, adding a new procedure or aborting the current one [3–9]. Some authors have reported that the impact of TEE in intraoperative management was most evident when used for Category I and II indications [5, 7, 9]. None of the mentioned studies was specifically conducted in thoracic surgery, and some included cardiac surgical patients [3, 7]. The lack of outcome trials looking

TABLE 20.1. Indication for TEE for intraoperative hemodynamic monitoring in high-risk patients.

Patients' characteristics	Type of surgery	Clinical setting
History of MI	Major vascular surgery	Difficult line insertion
History of unstable angina	Extensive tumor resection	Difficulties in estimating volume status
Positive stress test	Potential need for CPB	High hospital-specific morbidity and mortality for specific procedure
History of congestive heart failure		
Moderate or severe aortic stenosis	Massive blood loss	

TABLE 20.2. Use of TEE in noncardiac surgery.

Author	Number of patients	Indication	Type of surgery	Type of study	Change hemodynamic management	Change surgical management
Canty et al. [4]	13	I 4 (30%) II 9 (70%)	Gynecology, neurosurgery	Retrospective	9/13 (69%)	2/13 (14%)
Schulmeyer et al. [9]	98	II 98 (100%)	Abdominal, gynecology, urology	Prospective	47/98 (48%)	3/98 (3%)
Hofer et al. [6]	99	II 99 (100%)	Vascular, lung transplant, liver transplant, thoracic, orthopedic, reconstructive	Prospective cohort	54/99 (55%)	3/99 (3%)
Denault et al. [5]	155	I 44 (28%) II 57 (37%) III 54 (35%)	Vascular, neurosurgery, lung transplant	Retrospective	43/155 (27%)	10/155 (6%)
Suriani et al. [8]	123	II 123 (100%)	Vascular, abdominal, hepatic, thoracic, head and neck, urology	Retrospective	78/123 (63%)	2/123 (1%)
Kolev et al. [7]	224	I 48 (26%) II 151 (67%) III 15 (7%)	Cardiac 155 (69%), noncardiac 69 (31%)	Prospective multicenter cohort	25% of all interventions were uniquely based on TEE	9/224 (4%)
Brandt et al. [3]	66	I 66 (100%)	Cardiac and noncardiac	Retrospective	53 (80%)	15 (23%)

at the impact of the use of intraoperative TEE in noncardiac surgery makes it an interesting field for future research.

The impact of emergent TEE in the course of cardiac arrest in noncardiac patients has been specifically assessed in the operating room [10], as well as during in-hospital resuscitation [11]. In both settings, TEE has been reported to provide prompt diagnosis of the cause of circulatory arrest in 64–86% of the cases and to guide new surgical intervention in 54% of the patients. The ability of TEE to identify the etiology of cardiac arrest has been quantified with a sensitivity and specificity of 90 and 50%, respectively [11]. The release of new portable TEE equipment and the fact that TEE does not interfere with cardiopulmonary resuscitation (CPR) make TEE suitable to be integrated into Advanced Cardiac Life Support algorithms.

In North America, the need for TEE-certified anesthesiologists [12] and the availability of TEE equipment are the main limitations to the routine use of TEE outside of the cardiac operating room. Some authors have suggested that the use of a simplified focused TEE examination for transplant surgery may be adequate [13]. The American National Board of Echocardiography has recently defined a new certification process in basic perioperative TEE [14] that will potentially expand the use of TEE as an intraoperative monitoring tool.

Safety and Complications of TEE Probe Insertion

Although none of the studies mentioned above reported any complication related to the use of TEE, the insertion and manipulation of the TEE probe is not free of risks [15]. Major

complications in the use of TEE have been described and include esophageal dissection [16] and perforation [17].

Two large retrospective reviews on cardiac surgical patients undergoing intraoperative TEE reported incidences of major complications, respectively, of 0.2% of patients with no associated deaths [18] and of 0.1% with a mortality of 0.02% [19].

A careful assessment of the potential benefit of an intraoperative TEE examination against its potential complications must be performed in each patient.

Preoperative assessment is very important, and patient consent should be obtained whenever possible. A patient's history should be reviewed in order to rule out gastro-esophageal pathology. Esophageal narrowing should always be suspected with the presence of dysphagia. A radiological barium swallowing study remains the gold standard to rule out esophageal strictures [15] and should be performed whenever there is clinical suspicion.

The TEE probe should always be gently manipulated, and any force should be avoided in case of resistance to advancement into the esophagus. Esophageal perforation or tear may present soon after the removal of the probe with profuse bleeding from the pharynx or from a naso-gastric tube but is presents over 48 h after probe insertion [19].

Intubation of the esophagus, in the anesthetized patient, can be performed under direct vision or blindly with the help of jaw thrust maneuver. Esophageal intubation is a strong stimulus, and adequate depths of anesthesia and muscle paralysis are necessary to minimize the hemodynamic impact. It is standard practice in many centers to insert the TEE probe right after the placement of the endotracheal tube.

To minimize the risk of esophageal injury, the use of a pediatric TEE probe (Fig. 20.1) should be considered in very small-sized adults.

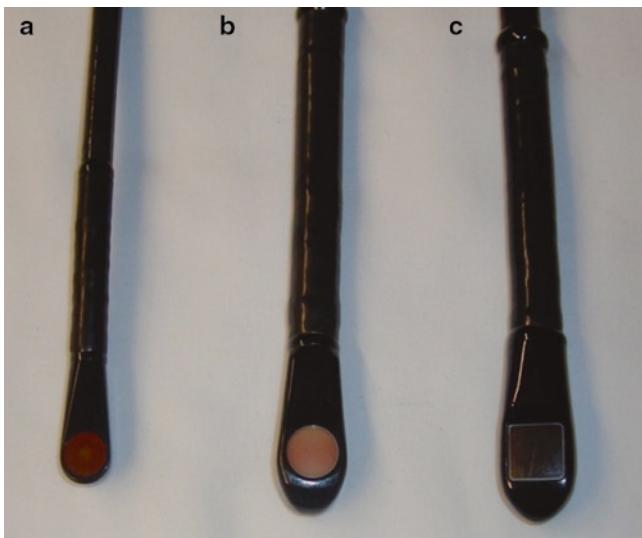


FIG. 20.1. *Probes*. The three types of TEE probes available: (a) pediatric; (b) adult omni-probe; (c) adult 3D.

Basic Hemodynamic Assessment

A complete intraoperative TEE assessment comprises the analysis of 20 standard views [20]. It should be performed at baseline and requires an expertise in TEE [12]. Current guidelines do not specify how often a complete examination should be repeated during the course of surgery and what views should be used for intraoperative hemodynamic monitoring.

After a complete baseline examination, many authors [5–7, 9] chose to leave the TEE probe in the stomach and use the transgastric short axis (TG SAX) view for the continuous assessment of LV function.

Visual analysis of the short axis of the LV in the TG SAX view provided adequate qualitative, online assessment of LV and RV function as well as an estimated volume status in many studies [5–7, 9].

TEE has been reported to predict postoperative myocardial infarction in patients following surgical myocardial revascularization [21], but its role in the detection of intraoperative myocardial ischemia in noncardiac surgery has been heavily questioned by negative studies [22].

A simplified approach to intraoperative TEE hemodynamic monitoring identifies five possible hemodynamic states (Table 20.3) [23]: normal, hypovolemia, LV systolic failure, LV diastolic failure, and right ventricular (RV) failure.

The differential diagnosis of hemodynamic status can be easily accomplished by combining the assessment of LV and RV function with the estimation of left atrial (LA) pressure.

An easy way of visually assessing LA pressure in mechanically ventilated patients is to determine the movement of the interatrial septum (IAS) during the respiratory cycle (Fig. 20.2) [24]. A fixed septum that never shifts left and right is a sign of increased LA pressure; this technique has been successfully validated against invasive monitoring [25]. We will discuss the assessment of LV and RV function in detail in the next paragraphs.

It has been reported that novices can achieve adequate confidence in assessing basic hemodynamics after a minimum number of supervised studies [26].

TABLE 20.3. Hemodynamic status.

Status	LVEDV	LV systolic function	LV diastolic function	RV systolic function	IAS in systole
Normal	Normal	Normal	Normal	Normal	Swing
Hypovolemia	Decreased	Normal or increased	Normal	Normal	Swing
LV failure	Increased	Decreased	Normal or abnormal	Normal	Fixed
LV diastolic failure	Decreased	Normal	Abnormal	Normal	Fixed
RV failure	Decreased	Normal	Normal or abnormal	Decreased	Fixed

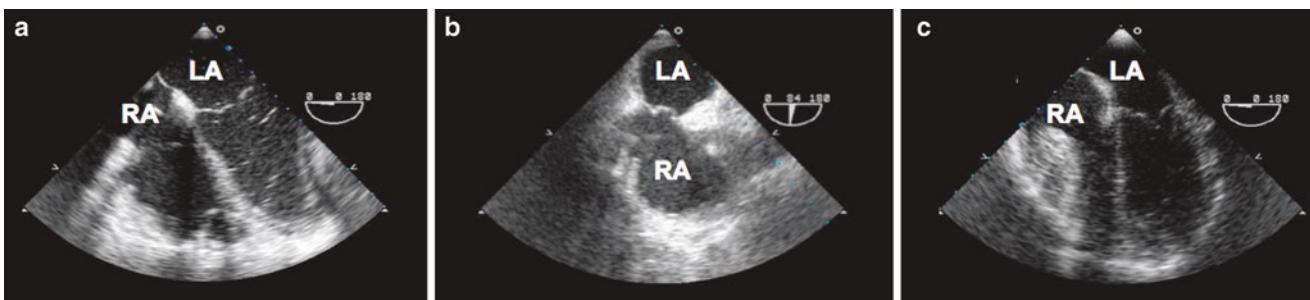


FIG. 20.2. *Interatrial septum shift*. In mechanically ventilated patients, the movement of the inter atrial septum (IAS) during the respiratory cycle reflects the pressure in the atrial chambers. High LA pressure results in a right bulge of the IAS that remains immobile during the respiratory cycle (a). Low LA pressure allow left and right IAS shifting that often presents as a “wrinkled” IAS (b). A fixed left bulge is characteristic of high RA pressure (c).

Assessment of Left Ventricular Function

Assessment of left ventricular (LV) function includes assessments of the LV preload, global and regional systolic function and diastolic function.

For the basic assessment of LV function, three standard views must be obtained: TG SAX, mid-esophageal four-chamber (ME 4C) view, and mid-esophageal two-chamber (ME 2C) view (Fig. 20.3).

The LV end-diastolic volume (LVEDV) is the best estimate of LV preload [23, 27]. LVEDV can be easily estimated by the linear measurement of the LV infero-anterior end-diastolic diameter (LVEDD) or, more precisely, the LV end-diastolic area (LVEDA) in the TG SAX view (Fig. 20.4) [28]. Complete emptying of the LV with virtualization of the LV cavity at end-systole is also a sign of decreased preload.

The LV ejection fraction (LVEF) is the percentage change in LV volume during the cardiac cycle and reflects the global LV systolic function. It is defined by the equation:

$$\text{LVEF} = [(LVEDV - LVESV)/LVEDV] \times 100, \text{ where LVESV is the LV end-systolic volume.}$$

TG SAX allows the visual assessment of global LV systolic function and was shown to correlate well with measured LVEF even when assessed by novices [29].

The quantification of LV function can be done in one (measuring diameters), two (measuring areas), or three dimensions (measuring volumes) (Fig. 20.4).

Linear measurement of LV function consists of the measurement of fractional shortening, or the percentage of change in the LV diameter during the cardiac cycle. It can be achieved by tracing a line across the maximum LV diameter in the TG SAX view, and although based on the movement of two points in the entire LV, it correlates with LVEF.

In the same view, the fractional area change (FAC), or the percentage change in the LV cross-sectional area during the cardiac cycle, can be measured. It is easily obtained by tracing the endocardial border of the LV in the end-systolic and the end-diastolic frames. FAC is easy to calculate and correlates well with the ejection fraction. Automatic endocardial border detection and automatic continuous FAC calculation software has been developed for continuous intraoperative monitoring but, after successful testing [30], never became widely used.

Global LV function can also be assessed by deriving the LV stroke volume (SV) from the Doppler measurement of the blood flow at the level of the LV outflow tract (LVOT) [31]. This technique is complex and may underestimate LV SV by underestimating the flow across the LVOT due to the mal-alignment of the Doppler beam and the LVOT flow.

LV volumes can be measured using the biplane method of the disks (modified Simpson's rule). It is based on the concept of dividing the LV cavity into a stack of 20 ellipsoids whose height is directly related to the length on the LV. After manually tracing the endocardial border in the end-diastolic and the

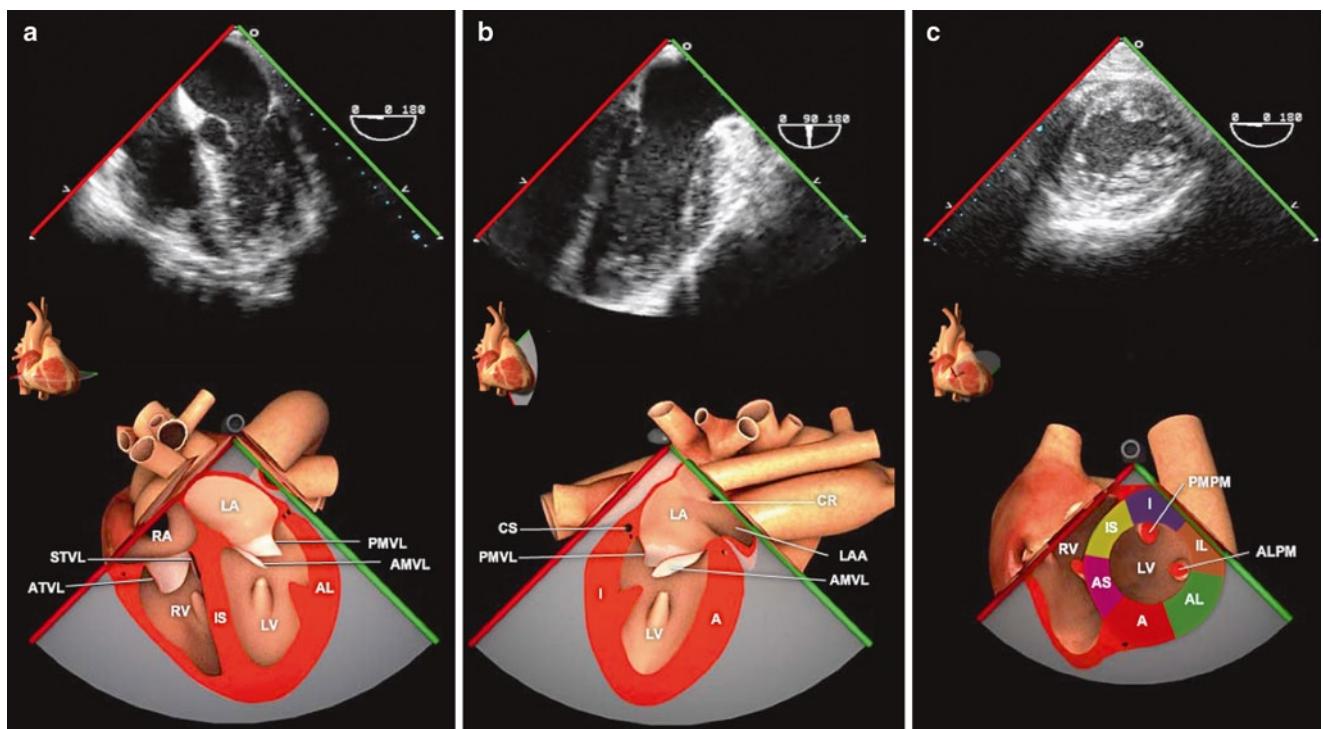
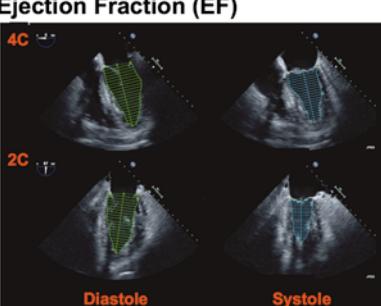
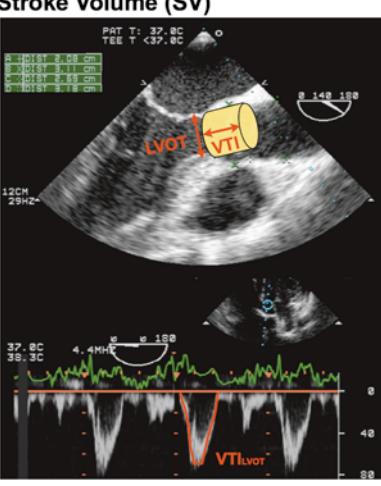


FIG. 20.3. *LV views.* Assessment of the left ventricular function requires obtaining the following three standard views: mid-esophageal four-chamber view (a), mid-esophageal two-chamber view (b), transgastric left ventricular mid short axis view (c) (Courtesy of Michael Corrin (<http://pie.med.utoronto.ca/TEE>)).

FIG. 20.4. Common methods and normals for quantification of LV function.

MEASURE	FORMULA	NORMAL VALUES
Fractional Shortening (FS) 	$[(LVEDD-LVESD)/LVEDD] \times 100$	FS: 25-45 % LVEDD: 4-5 cm
Fractional Area Change (FAC) 	$[(LVEDA-LVESA)/LVEDA] \times 100$	FAC: >55% LVEDA: 8-12 cm ²
Ejection Fraction (EF) 	Automatically Calculated based on Simpson's rule	EF: >55%
Stroke Volume (SV) 	$\pi(d_{LVOT}) \times VTI_{LVOT}$	SV: 50-70 ml

end-systolic frames of a ME 2C and a ME4C view, the modern echocardiographic machine automatically calculates LVEDV, LVESV, SV, and EF. This method is considered the gold standard [32], but it is time-consuming, requires good-quality images and necessitates experience with the technology.

To standardize the assessment of LV regional wall motion, the American Society of Echocardiography (ASE) classification divided the LV into 17 segments (Fig. 20.5) [32]. The segments are grouped into three levels, namely, the basal (six), mid ventricular (six) and apical (four), plus an apical cap. For a complete assessment of LV regional wall motion, all segments

should be displayed and individually assessed according to a rating scale (Table 20.4).

All of the segments are attributed to the main coronary arteries (Fig. 20.5) thus the analysis of segmental wall motion may allow the localization of individual coronary stenosis.

The TG SAX view allows the simultaneous visualization of the territories of the three main coronary arteries.

The quantitative assessment of diastolic dysfunction is complex and requires the assessment of multiple measures [33].

The advent of 3D TEE technology [34] offered the ability of directly and accurately measuring LV volumes [35, 36].

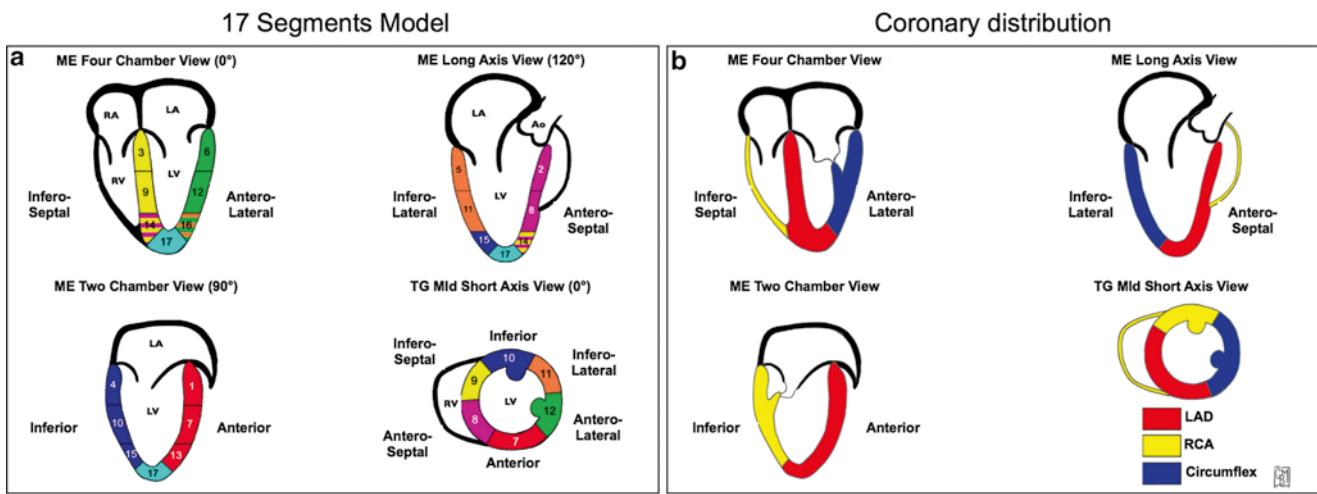


FIG. 20.5. 17 Segment model and coronary distribution. The diagram explains which left ventricular segments are seen in the most common TEE views of the LV (a). The relative coronary distribution (b). (Photo is courtesy of GM Busato).

TABLE 20.4. LV wall motion.

Definition	Standard terminology	Sign
Normal movement	Normal	++
Decreased movement	Hypokinetic	+
No movement	Akinetic	0
Outward bulging in systole	Dyskinetic	-
Fixed outward bulging	Aneurysmal	-

High-quality images of the LV are necessary and currently require the acquisition of a 3D dataset over four or eight heartbeats [37]. The acquired 3D volume “block” will subsequently be analyzed using an offline quantification software (Philips QLab™, Tomteq™).

The current software offers a semiautomatic method for the 3D reconstruction of the LV: given six anatomical landmarks on three orthogonal cuts of the full volume-scan of the LV on the systolic and the diastolic frames, the software elaborates a moving 3D cast of the LV cavity. The change in Global LV volume is immediately displayed on a graphic plot of the LV volume/time, together with measured LVEDV, LVESV, LVSV, and LVEF.

To allow the assessment of regional LV wall motion, the 3D cast of the LV cavity is divided into 17 pyramids according to the ASE 17 segment model [32], and the change in volume of each pyramid is plotted over time.

The volume/time plots of all segments are superimposed, allowing the assessment of dysynchrony.

The validity of 3D TEE in assessing LV dysynchrony has been extensively tested (Fig. 20.6) [38, 39].

The limitation of current 3D technology is the fact that it is not real-time and requires an expertise in acquiring and manipulating the datasets. Until newer, more powerful

machines will allow automatic LV reconstruction, the role of 3D TEE for the intraoperative monitoring of LV function seems to be limited.

Intraoperative diastolic dysfunction seems to correlate with poor postoperative outcome in noncardiac surgery [40]. It is unclear how to manage low grades of intraoperative diastolic dysfunction.

However, for a basic hemodynamic assessment, it is important to recognize an increased atrio-ventricular gradient that corresponds to a severe degree of diastolic dysfunction.

Normal transmural flow is characterized, in patients with normal sinus rhythm, by a biphasic pattern: early diastolic filling (*E* wave) and atrial contraction (*A* wave). The *E/A* waves ratio is normally within 1–1.5. With worsening of LV diastolic relaxability, such as with severe LV hypertrophy, the increased left atrio-ventricular gradient will result in an *E/A* waves ratio >2 with a peak velocity >90 cm/s [33].

Assessment of Right Ventricular Function

RV dysfunction is very common in patients with severe pulmonary disease [41]. TEE allows prompt diagnosis of RV dysfunction but requires an understanding of the pathophysiology of RV dysfunction and the complex 3D RV anatomy.

RV dysfunction is characterized by increased RA pressure, venous stasis, low cardiac output, LV diastolic dysfunction, and decreased LV preload [42]. It can be the result of RV pressure or volume overload and RV ischemia. The assessment of RV function includes assessments of the RV morphology and RV systolic function [43].

The right ventricle has a complex 3D architecture as it wraps around a conical LV. The RV can anatomically be divided into

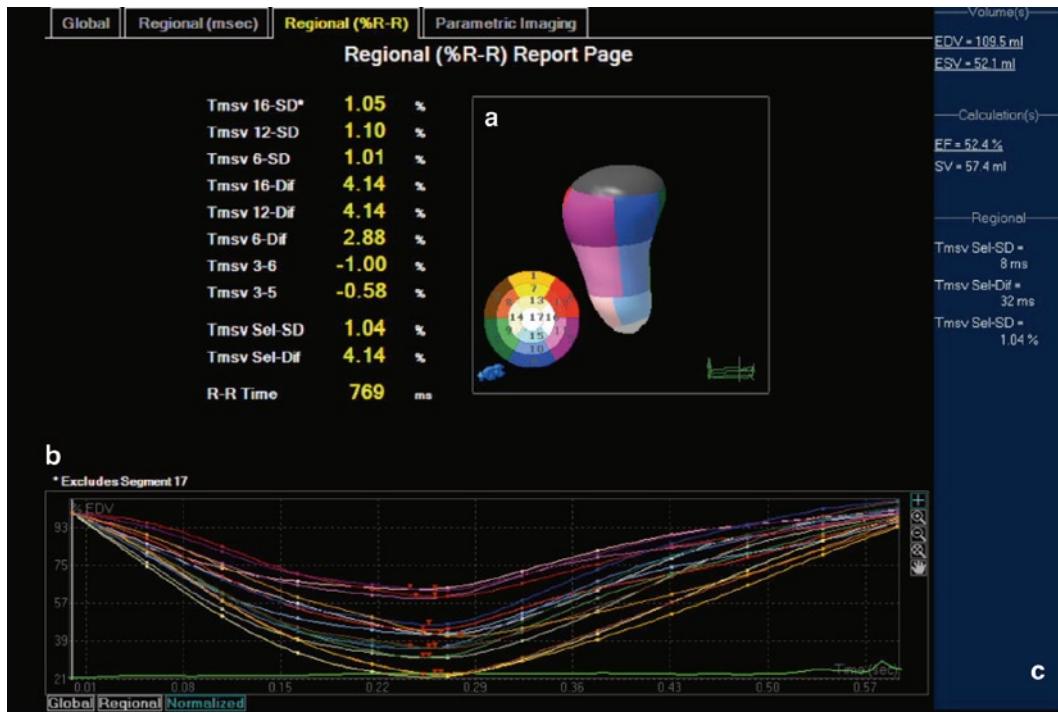


FIG. 20.6. 3D TEE LV assessment. (a) Left ventricular (LV) cast. The LV cavity is divided into 17 wedges each corresponding to one of the 17 segments. The change in shape of each on the 17 segments is plotted over time (b). The LV end-diastolic volume, end-systolic volume, and ejection fraction are automatically measured (c).

three parts: the inlet, composed by the tricuspid valve (TV), the chordae and the papillary muscles; the trabeculated muscular apex; and the outlet, composed by the smooth muscle outflow tract (RVOT).

The distinctive anatomical features of the RV are: a prominent muscular band from the free wall to the IVS, the proximity of the RV apex (moderator band), the more apical attachment of the septal leaflet of the tricuspid valve (TV) in comparison to the anterior leaflet of the mitral valve (MV) and the presence of more than two papillary muscles [44, 45].

The RV is a thin-walled structure, usually exposed to low pressures. The RV is very compliant and sensitive to changes in afterload; an acute increase in afterload results in RV dilatation. Chronic RV pressure overload causes concentric hypertrophy.

The basic TEE assessment of RV function requires the collection of the following three standard views: ME 4C, TG SAX, and mid-esophageal RV inflow–outflow (ME RV in–out) (Fig. 20.7).

The ME 4C view displays the triangular-shaped RV long axis. In this view, the RV end-diastolic area (RVEDA) can be measured and compared to the LVEDA (Fig. 20.8a). A normal RVEDA/LVEDA is <0.6 , and a RVEDA/LVEDA >1 indicates severe RV dilatation [44]. In the same view, we can observe that, as the RV dilates, it loses its triangular shape, and when

it is as big as the LV it starts to share the apex of the heart, to finally take over with severe dilatation (Fig. 20.8c) [46].

The ME RV in–out view displays the RV crescent shape. In this view, the RV inlet, free wall and outflow tract can be seen; linear measures include the RVOT diameter and the thickness of the RV free wall. A free wall thickness >5 mm at end-diastole indicates RV hypertrophy [32].

The TG SAX view displays the RV short axis as a crescent shape attached to a circular LV. With RV pressure overload, RV dilatation displaces the interventricular septum (IVS) toward the left. Distortion of the IVS is measured by the LV eccentricity index, which is the ratio of the LV infero-anterior and septo-lateral LV short axis diameters (Fig. 20.9a). With severe RV dilatation the LV loses its circular shape, instead becoming D-shaped (eccentricity index >1) (Fig. 20.9b).

RV ejection is generated by three separate mechanisms: inward movement of the RV free wall, apical displacement of the TV annulus, and traction of the free wall by contraction of the LV [47].

Qualitative assessment of RV function consists of visual determination of inward movement of the RV free wall in the ME 4C and the ME RV in–out views (Fig. 20.8).

In the ME 4C view, RV FAC can be measured as the percentage of change of the RV area during the cardiac cycle.

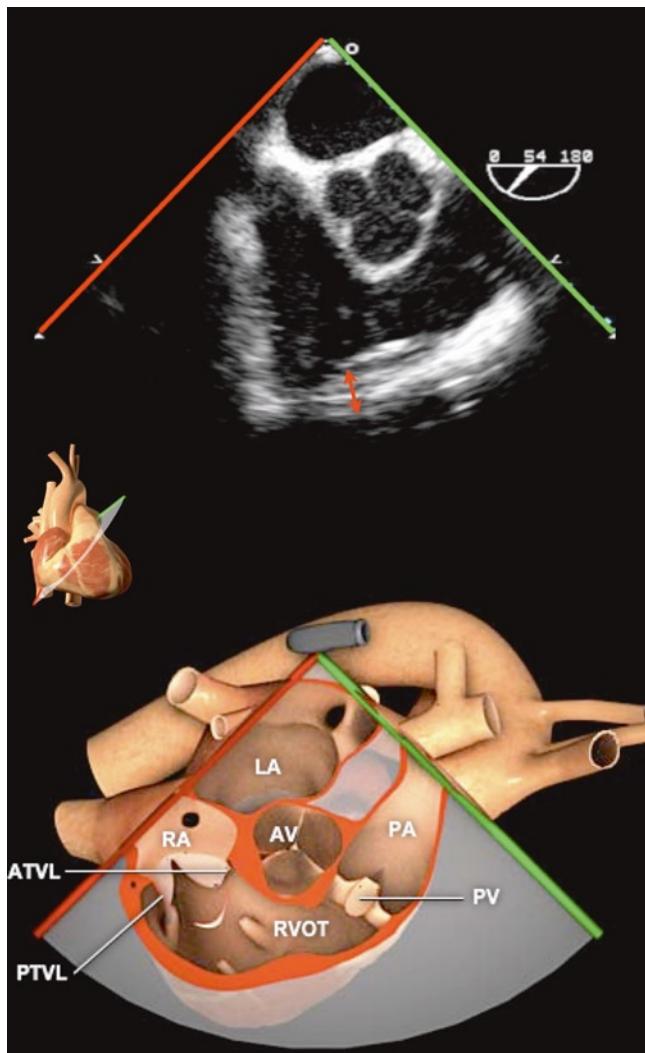


FIG. 20.7. *RV inflow-outflow view*. In this view, the ultrasound beam cuts the RV through its entire length. The arrow indicates RV wall thickness. (Photo is courtesy of Michael Corrin (<http://pie.med.utoronto.ca/TEE>)).

RV FAC well correlates with the RV EF measured by cardiac MRI [48].

In the same view, the TV annular plane systolic excursion (TAPSE) can be determined (Fig. 20.8b). In a normal heart, TAPSE is 1.5–2.0 cm, and a TAPSE <1.5 is associated with a poor outcome in patients with heart failure [49]. However, the TV annulus moves in a plane that is almost perpendicular to the TEE ultrasound beam, and this makes the accurate measurement of TAPSE with TEE very difficult.

The dilatation of the RV results in TV annular dilatation and regurgitation (TR) [50]. The severity of TR is not directly related to the severity of RV dysfunction. As the RV function deteriorates, the ability of RV to generate pressure is impaired; thus, a large, turbulent TR jet may turn into a low-velocity, laminar flow. In contrast, with RV remodeling following the treatment of RV pressure overload using, for example, pulmonary endarterectomy (PEA), an improvement in TR is observed [51].

Due to the complex shape of the RV, the RV volumes cannot be measured with standard TEE using polygonal models, as are commonly used for the LV.

Real-time 3D TEE overcomes some of the limitations of 2D TEE. A full volume 3D dataset of the RV is obtained over four heartbeats. The 3D block obtained can then be used for the offline measurement of right ventricular volume and function using special analytical software (4D RV-Function® application; TomTec Imaging Systems GmbH, Munich, Germany). 4D RV-Function® software allows the creation of a cast of the RV cavity and provides automatic measurement of RV volumes and EF (Fig. 20.10).

Although the use of RT 3D TEE in the assessment of right ventricular function has not been investigated, data from the real-time 3D transthoracic echocardiography (TTE) literature reported the feasibility of this technique [52–54]. Recent studies have shown a good correlation between 3D TTE and cardiac MRI [52, 53] with better reproducibility than 2D TTE [53] for the assessment of right ventricular volume and function in adults and children [55].



FIG. 20.8. *Assessment of RV function*. In the mid-esophageal four-chamber view, the right ventricle (RV) end-diastolic area can be measured and compared to LVEDA (a). The systolic displacement of the tricuspid valve annulus (TAPSE) (arrow) reflects RV function (b). With dilatation, the RV cavity loses its triangular shape and takes over the apex of the heart (c).

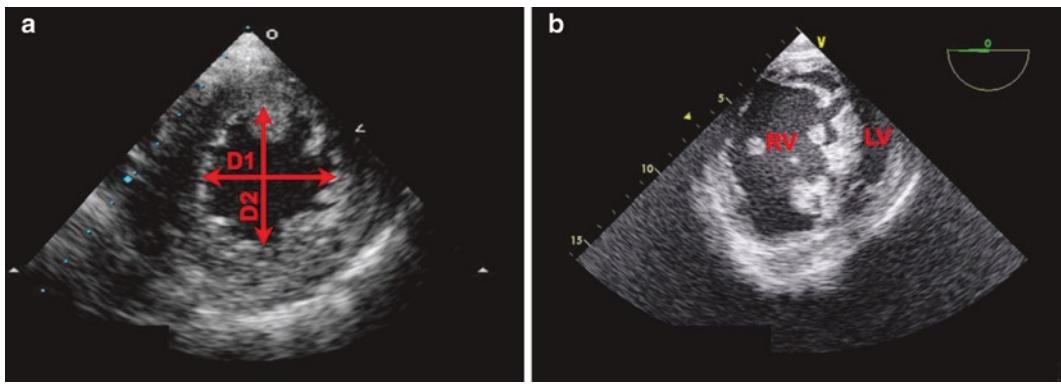


FIG. 20.9. *LV eccentricity*. The degree of flattening of the interventricular septum (IVS) can be quantified using the eccentricity index (EI). $EI = D1/D2$ where D1 is the infero-anterior and D2 is the latero-septal LV diameters (a). With RV dilatation flattening of the IVS results in a “D”-shaped LV cross section (b).

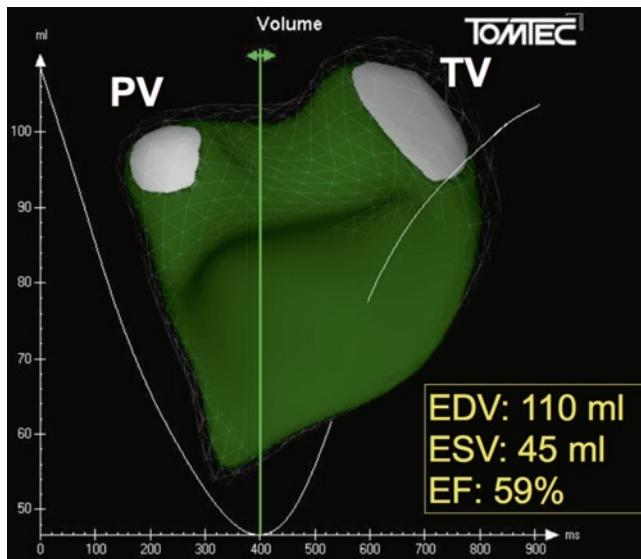


FIG. 20.10. *3D TEE RV assessment*. 4D RV-Function[®] application (TomTec Imaging Systems GmbH, Munich, Germany) allows offline processing of 3D TEE datasets and semi-automatic reconstruction of the RV cavity. In the RV cast tricuspid annulus (TV) and pulmonary valve annulus (PV) can be recognized.

TEE Assessment of PFO

Patent foramen ovale (PFO) is the result of the lack of fusion of the two interatrial septal flaps, the septum primum (left side) and the septum secundum (right side) (Fig. 20.11a). Until birth, an orifice in the septum secundum, covered by a mobile septum primum, allows maternal circulation through the heart.

At birth, as the left atrial pressure overcomes the right atrial pressure, the functional closure of the foramen ovale occurs. Through the years, a permanent fusion of the two flaps will seal the defect.

PFO is relatively common in the general population and is found in about 25% of autopsies [56].

TEE is the gold standard for the detection of PFO, with sensitivity between 80 and 100% and specificity of 100% [57–59].

To rule out the presence of a PFO, the TEE examination should focus on the careful inspection of the IAS in the ME 4C view. Once the IAS is visualized, the probe is rotated toward the right to bring the IAS into the middle of the screen. Given the normally small size, a PFO is unlikely noticed as a gap upon 2D examination. The color Doppler volume is then positioned to cover the IAS, and the nyquist limit is adjusted to 45–55 cm/s (Fig. 20.11b). While maintaining the IAS in the middle of the screen, the omniplane angle is rotated to slowly scan through the IAS from 0 to 120–130°.

To increase the sensitivity of the examination, a contrast study should be done. This consists of injecting an agitated saline solution through a central or a peripheral line and visualizing the shunt of air bubbles across the IAS.

Normally, the left atrial pressure is higher than that of the right atrial pressure, and even with the injection of agitated saline a shunt across the IAS cannot be seen. Provocative maneuvers such as a Valsalva or cough are used at the time of injection in order to increase the right atrial pressure (Fig. 20.11c) [60].

In the operating room on a ventilated patient, the sudden termination of a lung recruitment maneuver can cause an increase in the venous return and a subsequent increase in RA pressure. Thus, it is important to assess the transit of the contrast in the atria right at the end of a breath-hold.

A PFO is normally a benign cardiac abnormality, and in many patients, it may remain undiagnosed for their entire life. Factors that determine the clinical significance of a PFO are: size, cryptogenic strokes, RA to LA pressure gradient and flow from the inferior vena cava (IVC).

Smaller PFOs are less likely to be the cause of any symptoms, but they potentially allow paradoxical embolism, which may result in stroke [61]. The closure of the PFO in these

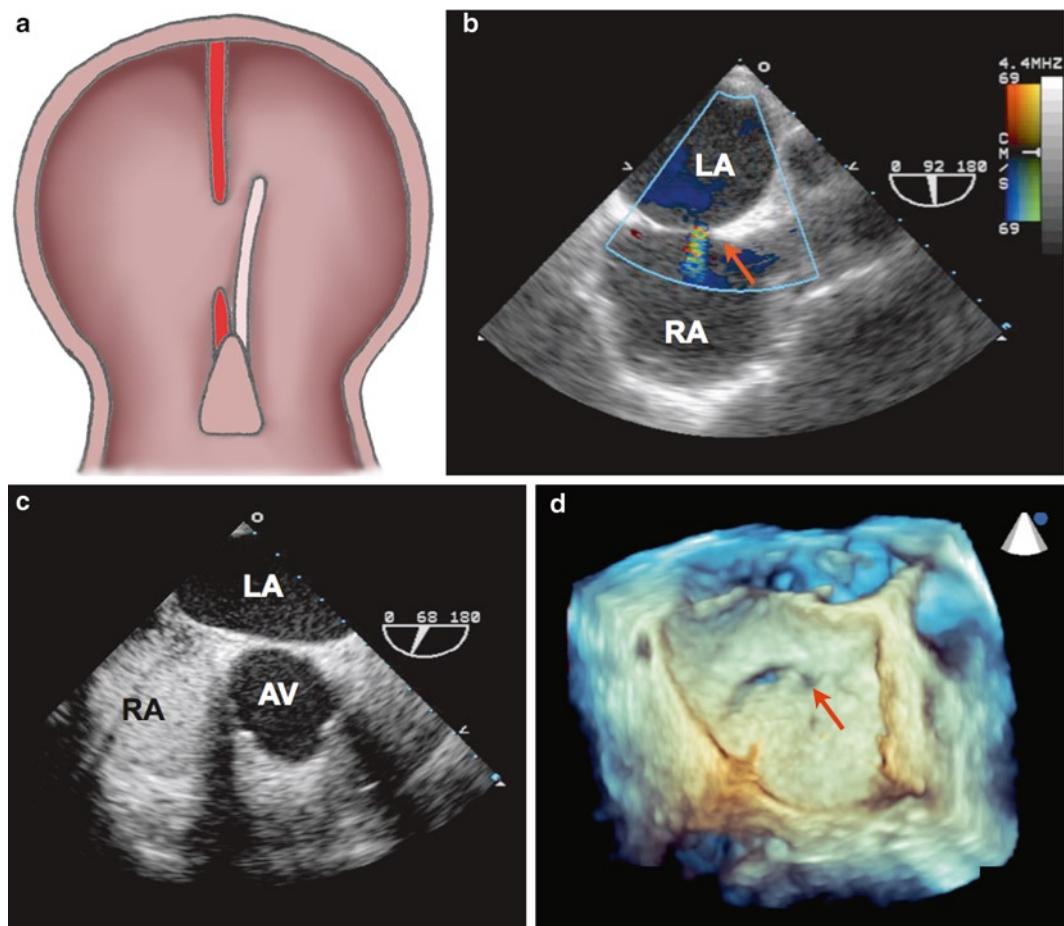


FIG. 20.11. *Patent foramen ovale*. Patent foramen ovale (PFO) is the result of lack of fusion of septum primum (left side) and septum secundum (right side) (a) (Photo is courtesy of GM Busato). Color Doppler allows identification of flow across a PFO that commonly creates a small left to right shunt (b). Agitated saline is the contrast medium of choice to confirm and detect the presence of PFO (c). 3D TEE can provide an en-face view of the inter atrial septum. (d) The PFO is seen from the left atrial side.

circumstances has to be considered as part of the prevention strategy.

With normal RA and LA pressures, a PFO results in a left-to-right shunt. All causes of increased RA pressure can revert the left-to-right shunt and result in hypoxia. An increase in RA pressure is very common in the thoracic surgical population with pulmonary disease and increased RV pressure overload. During major thoracic procedures such as lung transplant surgery, the clamping of the pulmonary artery results in a sudden increase in RV pressure that is reflected in the RA and can cause a hypoxic right-to-left shunt.

A diversion of the IVC flow toward the PFO due to altered anatomy has been described [62] after right pneumonectomy and can be the cause of otherwise unexpected severe hypoxia.

Percutaneous closure of the PFO has become the procedure of choice given its safety and minimal invasiveness [63]. On the other hand, the surgical closure of PFO, although a simple procedure, requires opening the heart chambers under cardio-pulmonary bypass (CPB).

During thoracic surgery, each patient with an intraoperative TEE diagnosis of PFO should be individually assessed. The detection of a continuous or intermittent right-to-left shunt may direct PFO closure, especially if the procedure involves the use of CPB anyway.

The best surgical management in the case of incidental intraoperative PFO finding in asymptomatic patients is not clear. In fact, a recent study [64] showed a cardiac surgical population with worse neurological outcomes after surgical PFO closure.

Specific Applications

Lung Transplant

The number of lung transplants has been increasing due to the increased demand for lung transplantation and the use of new techniques to expand the pool of donors [65, 66].

The increase in recipient ages and co-morbidities make optimal intraoperative anesthetic management more challenging. Cardiac abnormalities are commonly associated with severe pulmonary hypertension [67]. Coronary artery disease is present in up to 30% of patients with end-stage lung disease [68], and it is not uncommon for surgical coronary revascularization to be performed at the time of lung transplant.

Extracorporeal membrane oxygenators (ECMO) [69] and pump-less extracorporeal lung support (NovaLungTM) [70] have been increasingly used as bridges to transplantation (see Chap. 43).

Although its impact on patient outcome is not clear, TEE provides ideal intraoperative monitoring in the course of lung transplant [13]. The ASE considers the use of TEE for lung transplant surgery as a Category II indication, as lung transplant recipients are at high risk for intraoperative hemodynamic compromise and for problems with surgical anastomoses [2].

Table 20.5 summarizes the focus of the intraoperative TEE examination at different stages of the lung transplant.

The only direct contraindication to the insertion of the TEE probe in end-stage lung disease may be scleroderma, as it is associated in up to 30% of cases with esophageal strictures [71].

Some authors [13] have suggested inserting the TEE probe at the time of endotracheal intubation, as TEE may provide prompt diagnosis of the hemodynamic instability not uncommon immediately after the induction of anesthesia for lung transplant surgery [72]. The TEE examination should be started as soon as possible after induction, as the prolonged use of electrocautery after skin incision causes artifacts, making the interpretation of TEE images very difficult.

The TEE examination should first confirm the preoperative findings, as a significant amount of time may have passed from the preoperative assessment to the day of surgery.

The baseline TEE assessment should include a complete examination with special attention to RV function and the presence of intracardiac shunts. As previously discussed, a benign left-to-right shunt, such as a small PFO, may revert and cause hypoxia during the course of surgery as the right-sided pressure increases after the clamping of the pulmonary artery (PA) or during the manipulation of the heart. The surgeon may decide for the elective use of CPB in these circumstances to repair the PFO.

TEE assessment of extracorporeal devices requires an understanding of the basic circuits and surgical cannulation techniques. The use of TEE for this specific indication is not considered by current ASE guidelines.

NovaLungTM is an interventional lung-assist device, a pump-less membrane oxygenator, used in severe respiratory failure to provide CO₂ removal and oxygenation. The inflow cannula is placed percutaneously into the femoral artery and provides arterial blood flow to an oxygenator as the outflow cannula returns the oxygenated blood to the femoral vein. Normally the short NovalungTM cannulas are not seen with TEE. In the presence of severe RV pressure overload and hypoxia, NovolungTM has successfully been implanted between the main PA and the left upper pulmonary vein (LUPV), creating a septostomy-like shunt [70]. In these circumstances, TEE can easily visualize the cannulas and assess the flow (Fig. 20.12).

Whenever respiratory insufficiency is associated with heart failure, the use of ECMO becomes mandatory. An inflow cannula provides venous blood to an oxygenator that is pumped back

TABLE 20.5. TEE for lung transplant.

Induction	Dissection	PA clamping	Graft reperfusion	Post implant
TR and RVSP	LV, RV filling and function	RV function	Intracardiac air and LV function	TR and RVSP
Pulmonary veins				RV, LV function
LV, RV function				Pulmonary veins (all four) and pulmonary artery: R/O stenosis/thrombosis
IAS: R/O PFO and Intracardiac shunts				

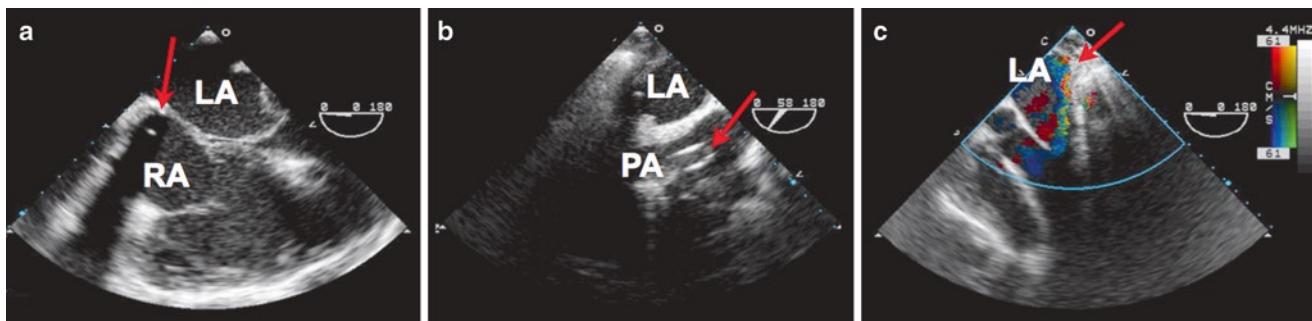


FIG. 20.12. *Cannulas*. TEE allows assessment of atrial cannulas for ECMO or NovaLung. (a) The arrow indicates the ECMO venous cannula in the right atrium. When the NovaLungTM is used for central bypass and decompression of the right heart chambers, the inflow cannula (flow to the NovaLung) is placed in the pulmonary artery (PA) (b) and the outflow cannula (return to the patient) is positioned in a pulmonary vein (here the left upper pulmonary vein) and drains into the left atrium (LA) (c).

to the patient's artery by a centrifugal pump. Femoral vessels are commonly used for cannulation, which can be performed percutaneously [73]. The short arterial cannula cannot usually be seen by TEE, but TEE is critical for guiding the positioning of the long venous cannula up to the RA.

Malpositioning of the venous cannula would result in impaired venous return and an inability to provide adequate arterial blood. In lung transplant recipients, TEE should assess the position and patency of the venous cannula at baseline and, when still necessary, after CPB.

During dissection of the native lungs, significant mechanical compression of the heart and distortion of great vessels can cause hemodynamic instability. TEE can promptly exclude other causes of hypotension, and manual compression of the heart chambers can easily be detected.

The use of CPB for lung transplantation, although not associated with increased mortality [74], certainly carries significant adverse effects such as systemic inflammatory syndrome and coagulopathy [75].

One indication for the elective use of CPB during lung transplantation is the need for simultaneous open-heart procedures. Given the lack of guidelines, the threshold for the use of CPB for lung transplant varies among different institutions. CPB is used in the presence of an occurrence of acute circulatory failure that usually presents as severe right ventricular failure at clamping of the PA. In these circumstances, TEE is a very sensitive tool for assessing RV function in real-time [46, 76], can detect early signs of RV failure after manual clamping of the PA and can prompt the use of CPB, thereby avoiding dangerous circulatory collapse [77].

After the completion of graft anastomoses, it is not uncommon to observe hypotension and ventricular failure at the unclamping of arterial and venous anastomoses. TEE commonly reveals a flush of air bubbles from the transplanted lung into the LV at this phase of the operation. Coronary air embolism, hypothermia, and metabolites from the preservative solution may cause severe LV failure at this stage.

TEE will assist weaning from CPB, as for all cardiac procedures, by monitoring the proper de-airing of the heart chambers and guiding the hemodynamic management. TEE allows the prompt diagnosis of post-CPB dynamic LVOT obstruction and is very useful in guiding hemodynamic management in this condition [78].

Severe pulmonary hypertension and RV failure has been observed after the administration of protamine; TEE is thus critical in monitoring RV function should, at this time and whenever during the course of the surgery, treatment with pulmonary vasodilators became necessary [79].

Following reperfusion of the grafts, a complete examination should be repeated. A lack of improvement of RV function following lung transplant has been associated with a poor outcome [80].

The visualization and measurement of flow in all of the pulmonary veins and pulmonary arteries is mandatory at this stage of surgery [81] and requires advanced TEE skills.

The proximal portion of the main pulmonary artery is seen with the PV and RVOT in the ME RV in-out view; in this view, its proximal diameter can be measured. Two other views should be used to assess the pulmonary artery: the mid-esophageal ascending aorta short axis (ME Asc Ao SAX) and the upper-esophageal aortic arch short axis (UE Ao Arch Sax) (Fig. 20.14).

The ME Asc Ao SAX displays the PA long axis at its bifurcation and the right PA (RPA). The left PA (LPA) is rarely seen as it is shadowed by the left main stem bronchus. In this view, the diameter of the PA anastomosis and the type of flow (laminar vs. turbulent) can be assessed. The UE Ao Arch Sax view shows the long axis of the PA, the bifurcation and the RPA, and it allows optimal alignment of the Doppler beam to the PA flow and the measurement of the flow velocity. Whenever the quality of TEE images is suboptimal or LPA could not be displayed, pericardial echocardiography should be considered [82].

Pulmonary veins can be seen starting from two standard views: ME 2C and the mid-esophageal bicaval view (ME BiC). From the ME 2C view while slightly pulling the TEE probe, we can visualize the LUPV that lies right above the LA appendage. By advancing the probe 1–2 cm, the left lower pulmonary vein (LLPV) can be visualized. LLPV is more difficult to see and often merges with the LUPV to form a common vessel. By rotating the probe toward the right, the right upper pulmonary vein (RUPV) is visualized as it enters the LA just above the SVC. By advancing the probe and slightly rotating it to the right, the right lower pulmonary vein (RLPV) can be seen. In all of the mentioned views, the diameter as well as the flow of all PV can be measured. The stenosis and thrombosis of pulmonary venous (PV) anastomoses has been reported by several authors [83], with incidences of PA stenosis around 7% [84] and PV stenosis around 10% [85]. A diameter <5 mm and a peak systolic velocity >1 m/s are considered cut-off for the definition of PV stenosis (Fig. 20.13) [83].

The gold standard for the diagnosis of PV stenosis and thrombosis remains angiography.

Heart–Lung Transplant

Heart–lung transplant is offered to some patients with congenital heart disease and/or pulmonary hypertension [86]. These patients may present to the operating room with ECMO or NovaLung™. The aim of the TEE examination is to guarantee the safe transition to full CPB.

The baseline assessment includes assessments of the cannulas' positioning and flows. The surgery consists of the en block transplant of heart and lungs requiring four anastomoses: the trachea, ascending aorta, and inferior and superior vena cava. After weaning from CPB, flow in the IVC and SVC rule out stenoses [87]. In these cases, there is no risk of the stenosis of the pulmonary vein and PA anastomoses as they are not affected by the surgery.

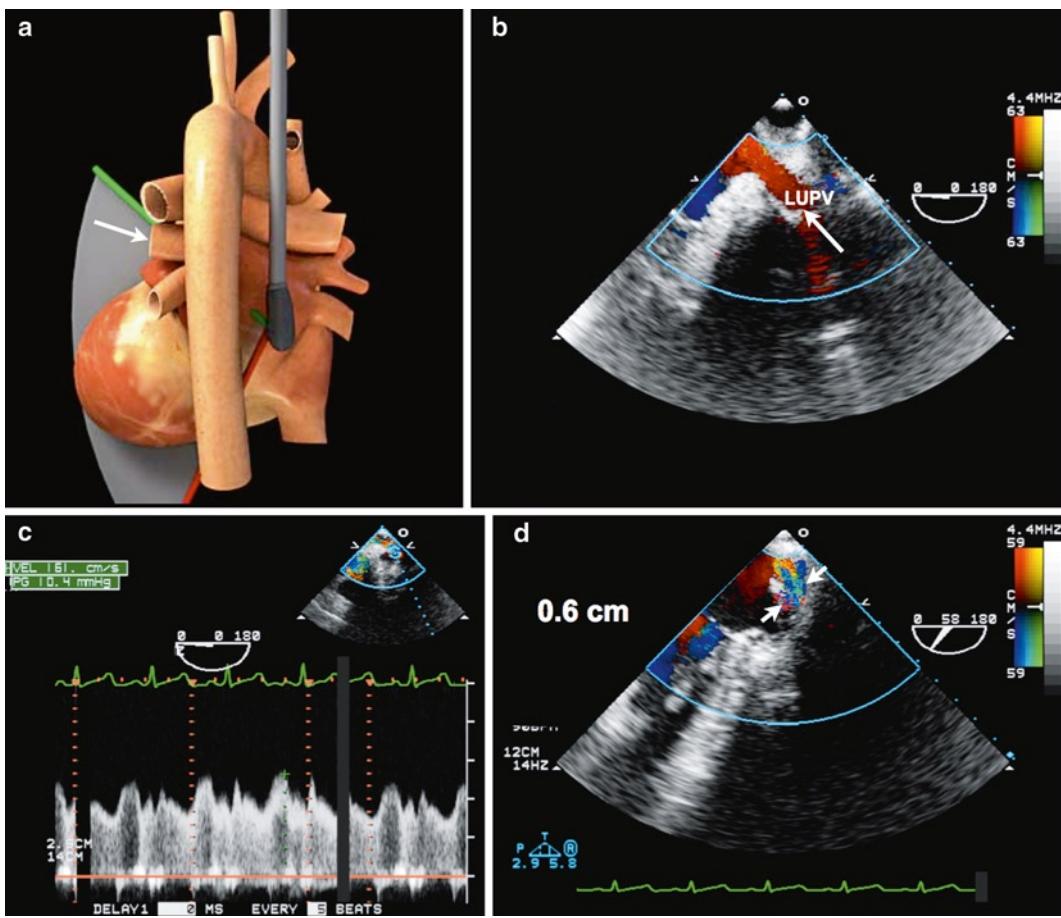
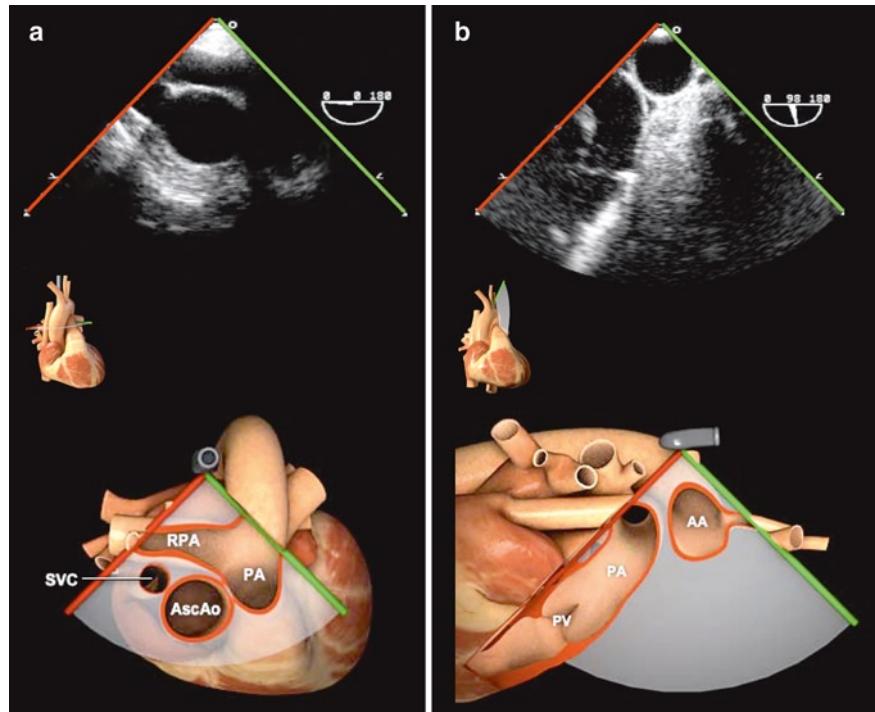


FIG. 20.13. *TEE views of the pulmonary veins.* After double lung transplant, the four pulmonary veins should be examined (a) (Photo is courtesy of Michael Corrin (<http://pie.med.utoronto.ca/TEE>)). The left upper pulmonary vein (arrow) is the easiest to image (b). Turbulent flow may correlate with narrowing (d) and normally leads to flow acceleration (c).

FIG. 20.14. *TEE views of pulmonary arteries.* The mid-esophageal ascending aorta short axis view displays the long axis of the main, right, and proximal left pulmonary arteries (a). The upper-esophageal aortic arch short axis view displays the long axis of the main and right pulmonary arteries (b). This view allows good alignment to pulmonary artery flow for Doppler measurements. (Photo is courtesy of Michael Corrin (<http://pie.med.utoronto.ca/TEE>)).



Prolonged CPB may lead to significant edema of the heart and mediastinal structures; RV compression and hypotension may prevent chest closure after heart-lung transplant.

Pulmonary Embolism

The use of TEE for pulmonary embolectomy is considered a Category II indication by current ASA guidelines. Although there are no outcome studies available assessing this specific application of TEE, it has been successfully used in the diagnosis of acute pulmonary embolism (PE) both in the operating room [88] and in the course of CPR [89].

Surgical pulmonary embolectomy is more often performed in tertiary care centers and consists of suctioning the fresh thrombi from the main PA on CPB and often positioning of an IVC filter [90].

Chronic PE leads to pulmonary hypertension and ultimately RV failure. Pulmonary thrombo-endarterectomy (PTE) is considered the definite treatment of pulmonary hypertension in these circumstances. It is commonly performed on CPB with deep hypothermic circulatory arrest and consists of the removal of thrombi and a thorough endoarterectomy of the pulmonary circulation [91]. TEE is commonly a part of the intraoperative

monitoring for both procedures [92]. Table 20.6 summarizes the focus of intraoperative TEE for PTE.

A complete TEE examination is performed at baseline and it is focused on the detection of thrombi, the assessment of RV function, and the exclusion of other causes of pulmonary hypertension.

TEE can easily see fresh thrombi in the IVC, RA, RV, and proximal PA (Fig. 20.15). The presence of free-floating thrombi in the RA is associated with PE in the great majority of patients [93].

However, the ability of TEE in localizing thrombi in the pulmonary circulation is limited by the fact that TEE can only image the proximal pulmonary circulation and that the LPA is often completely shadowed by the left main stem bronchus. PE causes RV pressure overload that manifests with PA, RV dilatation, and TR (Fig. 20.16) [43]. RV dysfunction in the

TABLE 20.6. TEE for pulmonary embolectomy.

Induction	Weaning from CPB	PA clamping
TR and RVSP	De-airing of RV and LV	TR and RVSP
LV, RV function	RV, LV function	RV function
IAS: R/O PFO and intracardiac shunts	RV, LV function	R/O PA clots
R/O clots in RA, RV and PA		

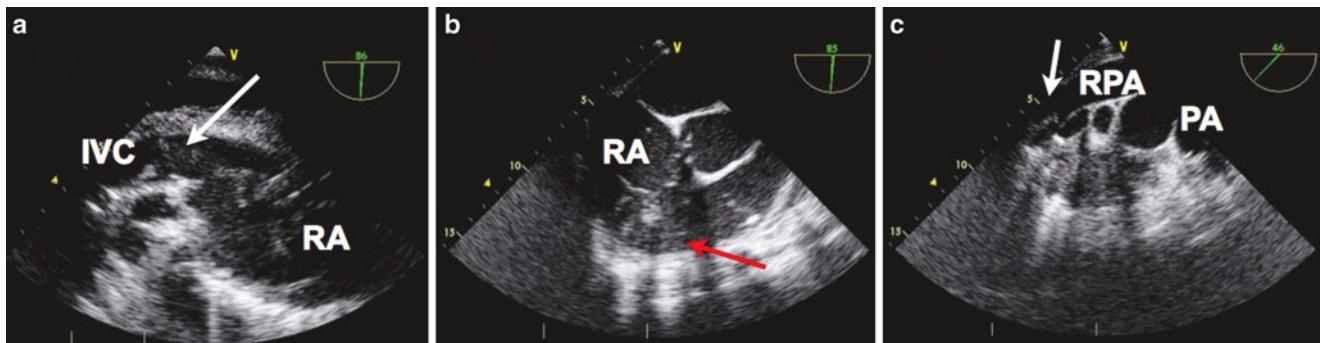


FIG. 20.15. *Pulmonary embolism.* Presence of thrombi (arrow) in the inferior vena cava (a) and right ventricle (arrow) (b) very often correlates with pulmonary embolism (c).

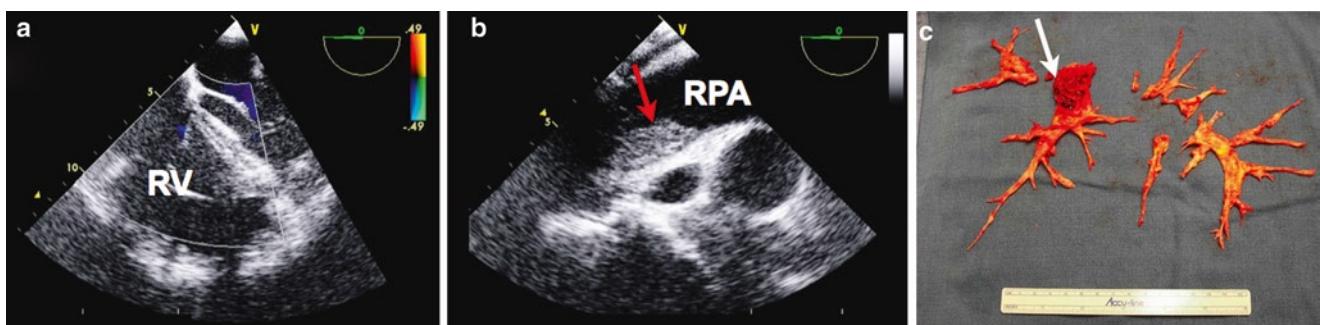


FIG. 20.16. *Chronic pulmonary embolism.* Chronic pulmonary embolism results in pulmonary hypertension and right ventricular overload and dilatation (a). TEE can detect thrombi in the right PA (b, arrow). Pulmonary endarterectomy consists in removal of thrombi (arrow) and thorough endoarterectomy of the pulmonary circulation (c). (Photo is courtesy of Dr. M. De Perrot.)

course of PE has found to be associated with poor in-hospital outcomes [94]. The assessment of PFO is crucial due to the high risk of paradoxical emboli and, when present, predisposes to poor outcomes [95].

Basic grading of TR at baseline is very important, and it can be performed in the ME 4C and the RV in-out views. It consists of tracing the area of the TR jet and measuring the TR jet width at the level of the TV leaflets (vena contracta) [96]. In the ME RV in-out view, Doppler measurement of the TV regurgitant jet peak velocity allows the calculation of the RV end-systolic pressure (RVSP). Due to the mal-alignment of the Doppler beam and the TR jet, the RVSP is often underestimated with TEE.

At separation from CPB, TEE is used to guide the careful de-airing of the heart chambers and for hemodynamic management.

A complete examination is then repeated at the end of the surgery and is needed to grade RV function, TR, and RVSP.

Improvements in RV function and TR are signs of a successful surgery; in contrast, the persistence of RV dysfunction and the lack of improvement in TR do not constitute a reason for further surgery, as remodeling of the RV and improvement in TR often take weeks after PTE [97, 98].

Lung and Mediastinal Masses

TEE has been successfully used in the diagnosis and management of mediastinal masses:

TEE allowed the incidental diagnosis of mediastinal tumors in patients referred for drainage of pericardial effusion [98, 99]; TEE identified the presence of surgical sponges [100] and led to the diagnosis of esophageal cancer [101]; finally, the resection of large anterior [102] and middle [103] mediastinal tumors greatly benefited from intraoperative TEE.

TEE can assess all cardiac chambers and may define extrinsic compression and tumor invasion. As previously reported [99], the presence of mediastinal masses predisposes to circulatory collapse at the induction of anesthesia, which is a Category I indication for the use of TEE.

In patients with cancer of the left lung, TEE has been used in the preoperative assessment of the invasion of the thoracic aortic wall and showed very high sensitivity when compared to CT scan [104].

Clinical Case Discussion

Case: A 54-year-old female presents for double lung transplantation. The patient has a history of end-stage lung disease secondary to bronchiolitis obliterans. Preoperative echocardiogram showed normal RV and LV function, normal valves and RVSP of 34 mmHg. MUGA confirmed good LV function and excluded myocardial ischemia. After a smooth induction of anesthesia, a TEE probe is inserted. The ME 4C view is displayed. Color Doppler analysis is performed on the MV (Fig. 20.17).

- Is there anything abnormal with the MV?

The base of the posterior mitral valve leaflet is calcified, a mass attached to its atrial aspect (arrow).

- What could be the differential diagnosis of this pathology?
- Thrombus, infective vegetation or tumor.
- What should be done to better assess the MV?
- Obtain multiple views of the mitral valve with and without color Doppler.
- What may be the surgical implications of this finding?

Use CPB to surgically explore the mitral valve and eventually perform valve surgery. Gentle manipulation of the heart should prevent dislodging of the mass attached to the mitral valve.

A double lung transplant is performed without CPB. No surgery is performed on the MV nor it is surgically inspected.

- What should be the focus of immediate post CPB TEE examination?

Assess mitral valve for regurgitation and mass on the posterior leaflet.

After weaning from CPB, the patient is hypotensive regardless high doses of inotropes.

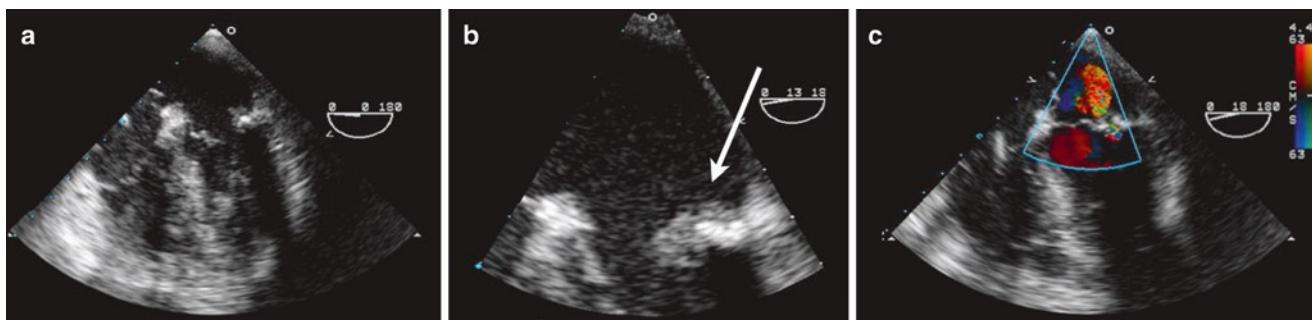
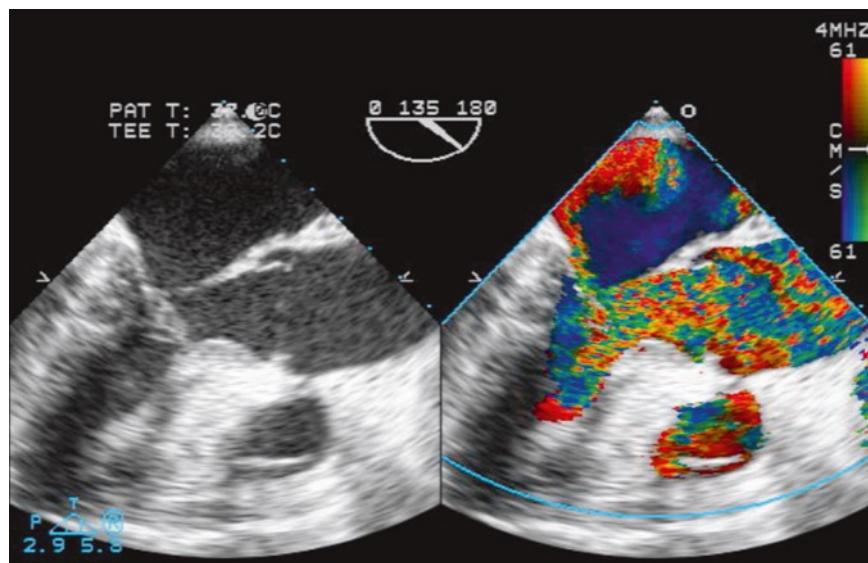


FIG. 20.17. Case discussion. (a) Mid-esophageal four-chamber view, (b) zoom on mitral valve, (c) color Doppler of the mitral valve.

FIG. 20.18. *Case discussion.* Mid-esophageal aortic valve long axis view: color Doppler of the LVOT and mitral valve.



TEE shows the abnormal flow in the LVOT and severe MR (Fig. 20.18).

- What is happening?

This is a case of dynamic LVOT obstruction and systolic motion of the anterior mitral valve leaflet with severe mitral regurgitation. The hyperdynamic, hypertrophic left ventricle generates a high pressure gradient across the LVOT and for a Bernoulli effect sucks in the anterior leaflet of the mitral valve.

- What is the treatment?

Volume load, avoid inotropes, short-acting beta-blockers, and vasopressor.

The postoperative course is complicated by decreased level of consciousness. Seven days postoperatively, a CT scan of the brain showed multiple strokes. We cannot exclude that embolization of material from the MV mass may have contributed to the clinical picture.

References

1. Mahmood F, Christie A, Matyal R. Transesophageal echocardiography and noncardiac surgery. *Semin Cardiothorac Vasc Anesth.* 2008;12(4):265–89.
2. Practice guidelines for perioperative transesophageal echocardiography. A report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology.* 1996;84(4):986–1006.
3. Brandt RR, Oh JK, Abel MD, Click RL, Orszulak TA, Seward JB. Role of emergency intraoperative transesophageal echocardiography. *J Am Soc Echocardiogr.* 1998;11(10):972–7.
4. Carty DJ, Royse CF. Audit of anaesthetist-performed echocardiography on perioperative management decisions for non-cardiac surgery. *Br J Anaesth.* 2009;103(3):352–8.
5. Denault AY, Couture P, McKenty S, et al. Perioperative use of transesophageal echocardiography by anesthesiologists: impact in noncardiac surgery and in the intensive care unit. *Can J Anaesth.* 2002;49(3):287–93.
6. Hofer CK, Zollinger A, Rak M, et al. Therapeutic impact of intra-operative transoesophageal echocardiography during non-cardiac surgery. *Anaesthesia.* 2004;59(1):3–9.
7. Kolev N, Bräse R, Swanevelder J, et al. The influence of transoesophageal echocardiography on intra-operative decision making. A European multicentre study. European Perioperative TOE Research Group. *Anaesthesia.* 1998;53(8):767–73.
8. Suriani RJ, Neustein S, Shore-Lesserson L, Konstadt S. Intraoperative transesophageal echocardiography during noncardiac surgery. *J Cardiothorac Vasc Anesth.* 1998;12(3):274–80.
9. Schulmeyer MC, Santelices E, Vega R, Schmied S. Impact of intraoperative transesophageal echocardiography during noncardiac surgery. *J Cardiothorac Vasc Anesth.* 2006;20(6):768–71.
10. Memtsoudis SG, Rosenberger P, Loeffler M, et al. The usefulness of transesophageal echocardiography during intraoperative cardiac arrest in noncardiac surgery. *Anesth Analg.* 2006;102(6):1653–7.
11. van der Wouw PA, Koster RW, Delemarre BJ, de Vos R, Lampe-Schoenmaeckers AJ, Lie KI. Diagnostic accuracy of transesophageal echocardiography during cardiopulmonary resuscitation. *J Am Coll Cardiol.* 1997;30(3):780–3.
12. Cahalan MK, Abel M, Goldman M, et al. American Society of Echocardiography and Society of Cardiovascular Anesthesiologists task force guidelines for training in perioperative echocardiography. *Anesth Analg.* 2002;94(6):1384–8.
13. Serra E, Feltracco P, Barbieri S, Forti A, Ori C. Transesophageal echocardiography during lung transplantation. *Transplant Proc.* 2007;39(6):1981–2.
14. <http://www.echoboards.org/pte/basicexam.html>. Accessed. May 2010.
15. Cote G, Denault A. Transesophageal echocardiography-related complications. *Can J Anaesth.* 2008;55(9):622–47.

16. El-Chami MF, Martin RP, Lerakis S. Esophageal dissection complicating transesophageal echocardiogram-the lesson to be learned: do not force the issue. *J Am Soc Echocardiogr.* 2006;19(5):e5–7. 579.
17. Augoustides JG, Hosalkar HH, Milas BL, Acker M, Savino JS. Upper gastrointestinal injuries related to perioperative transesophageal echocardiography: index case, literature review, classification proposal, and call for a registry. *J Cardiothorac Vasc Anesth.* 2006;20(3):379–84.
18. Kallmeyer IJ, Collard CD, Fox JA, Body SC, Shernan SK. The safety of intraoperative transesophageal echocardiography: a case series of 7200 cardiac surgical patients. *Anesth Analg.* 2001;92(5):1126–30.
19. Piercy M, McNicol L, Dinh DT, Story DA, Smith JA. Major complications related to the use of transesophageal echocardiography in cardiac surgery. *J Cardiothorac Vasc Anesth.* 2009; 23(1):62–5.
20. Shanewise JS, Cheung AT, Aronson S, et al. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. *J Am Soc Echocardiogr.* 1999;12(10):884–900.
21. Comunale ME, Body SC, Ley C, et al. The concordance of intraoperative left ventricular wall-motion abnormalities and electrocardiographic S-T segment changes: association with outcome after coronary revascularization. Multicenter Study of Perioperative Ischemia (McSPI) Research Group. *Anesthesiology.* 1998;88(4):945–54.
22. Eisenberg MJ, London MJ, Leung JM, et al. Monitoring for myocardial ischemia during noncardiac surgery. A technology assessment of transesophageal echocardiography and 12-lead electrocardiography. The Study of Perioperative Ischemia Research Group. *JAMA.* 1992;268(2):210–6.
23. Royse CF. Ultrasound-guided haemodynamic state assessment. *Best Pract Res Clin Anaesthesiol.* 2009;23(3):273–83.
24. Kusumoto FM, Muhiudeen IA, Kuecherer HF, Cahalan MK, Schiller NB. Response of the interatrial septum to transatrial pressure gradients and its potential for predicting pulmonary capillary wedge pressure: an intraoperative study using transesophageal echocardiography in patients during mechanical ventilation. *J Am Coll Cardiol.* 1993;21(3):721–8.
25. Royse CF, Royse AG, Soeding PF, Blake DW. Shape and movement of the interatrial septum predicts change in pulmonary capillary wedge pressure. *Ann Thorac Cardiovasc Surg.* 2001;7(2):79–83.
26. Royse CF, Seah JL, Donelan L, Royse AG. Point of care ultrasound for basic haemodynamic assessment: novice compared with an expert operator. *Anaesthesia.* 2006;61(9):849–55.
27. Della Rocca G, Costa MG, Coccia C, et al. Continuous right ventricular end-diastolic volume in comparison with left ventricular end-diastolic area. *Eur J Anaesthesiol.* 2009;26(4):272–8.
28. Scheuren K, Wente MN, Hainer C, et al. Left ventricular end-diastolic area is a measure of cardiac preload in patients with early septic shock. *Eur J Anaesthesiol.* 2009;26(9):759–65.
29. Hope MD, de la Pena E, Yang PC, Liang DH, McConnell MV, Rosenthal DN. A visual approach for the accurate determination of echocardiographic left ventricular ejection fraction by medical students. *J Am Soc Echocardiogr.* 2003;16(8):824–31.
30. Spencer KT, Lang RM, Kirkpatrick JN, Mor-Avi V. Assessment of global and regional left ventricular diastolic function in hypertensive heart disease using automated border detection techniques. *Echocardiography.* 2003;20(7):673–81.
31. London MJ. Assessment of left ventricular global systolic function by transoesophageal echocardiography. *Ann Card Anaesth.* 2006;9(2):157–63.
32. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr.* 2005;18(12):1440–63.
33. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr.* 2009;22(2): 107–33.
34. Fischer GW, Salgo IS, Adams DH. Real-time three-dimensional transesophageal echocardiography: the matrix revolution. *J Cardiothorac Vasc Anesth.* 2008;22(6):904–12.
35. Mor-Avi V, Jenkins B, Kuhl H, et al. Real-time 3D echocardiographic quantification of left ventricular volumes: multicenter study for validation with magnetic resonance imaging and investigation of sources of error. *JACC Cardiovasc Imaging.* 2008;1:413–23.
36. Pouleur AC, le Polain de Waroux JB, Pasquet A, et al. Assessment of left ventricular mass and volumes by three-dimensional echocardiography in patients with or without wall motion abnormalities: comparison against cine magnetic resonance imaging. *Heart.* 2008;94(8):1050–7.
37. Salgo IS. Three-dimensional echocardiographic technology. *Cardiol Clin.* 2007;25(2):231–9.
38. Vieira ML, Cury AF, Naccarato G, et al. Analysis of left ventricular regional dyssynchrony: comparison between real time 3D echocardiography and tissue Doppler imaging. *Echocardiography.* 2009;26(6):675–83.
39. Liodakis E, Al Sharef O, Dawson D, Nihoyannopoulos P. The use of real time three dimensional echocardiography for assessing mechanical synchronicity. *Heart.* 2009;95(22):1865–71.
40. Matyal R, Hess PE, Subramaniam B, et al. Perioperative diastolic dysfunction during vascular surgery and its association with post-operative outcome. *J Vasc Surg.* 2009;50(1):70–6.
41. Vizza CD, Lynch JP, Ochoa LL, Richardson G, Trulock EP. Right and left ventricular dysfunction in patients with severe pulmonary disease. *Chest.* 1998;113(3):576–83.
42. Pedoto A, Amar D. Right heart function in thoracic surgery: role of echocardiography. *Curr Opin Anaesthesiol.* 2009;22(1): 44–9.
43. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. *Circulation.* 2008;117(13):1717–31.
44. Vieillard-Baron A. Assessment of right ventricular function. *Curr Opin Crit Care.* 2009;15(3):254–60.
45. Davlouros PA, Niwa K, Webb G, Gatzoulis MA. The right ventricle in congenital heart disease. *Heart.* 2006;92 Suppl 1:i27–38.
46. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: I. Anatomy, physiology, and assessment. *Anesth Analg.* 2009;108(2): 407–21.

47. Haddad F, Hunt SA, Rosenthal DN, Murphy DJ. Right ventricular function in cardiovascular disease, part I: anatomy, physiology, aging, and functional assessment of the right ventricle. *Circulation*. 2008;117(11):1436–48.
48. Anavekar NS, Gerson D, Skali H, Kwong RY, Yucel EK, Solomon SD. Two-dimensional assessment of right ventricular function: an echocardiographic-MRI correlative study. *Echocardiography*. 2007;24(5):452–6.
49. Meluzin J, Spinarova L, Hude P, et al. Prognostic importance of various echocardiographic right ventricular functional parameters in patients with symptomatic heart failure. *J Am Soc Echocardiogr*. 2005;18(5):435–44.
50. Fukuda S, Gillinov AM, McCarthy PM, et al. Determinants of recurrent or residual functional tricuspid regurgitation after tricuspid annuloplasty. *Circulation*. 2006;114(1 Suppl):I582–7.
51. Rogers JH, Bolling SF. The tricuspid valve: current perspective and evolving management of tricuspid regurgitation. *Circulation*. 2009;119(20):2718–25.
52. Niemann PS, Pinho L, Balbach T, et al. Anatomically oriented right ventricular volume measurements with dynamic three-dimensional echocardiography validated by 3-Tesla magnetic resonance imaging. *J Am Coll Cardiol*. 2007;50(17):1668–76.
53. Gopal AS, Chukwu EO, Iwuchukwu CJ, et al. Normal values of right ventricular size and function by real-time 3-dimensional echocardiography: comparison with cardiac magnetic resonance imaging. *J Am Soc Echocardiogr*. 2007;20(5):445–55.
54. Kjaergaard J, Petersen CL, Kjaer A, Schaadt BK, Oh JK, Hassager C. Evaluation of right ventricular volume and function by 2D and 3D echocardiography compared to MRI. *Eur J Echocardiogr*. 2006;7(6):430–8.
55. Lu X, Nadvoretskiy V, Bu L, et al. Accuracy and reproducibility of real-time three-dimensional echocardiography for assessment of right ventricular volumes and ejection fraction in children. *J Am Soc Echocardiogr*. 2008;21(1):84–9.
56. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc*. 1984;59(1):17–20.
57. Schneider B, Zienkiewicz T, Jansen V, Hofmann T, Noltenius H, Meinertz T. Diagnosis of patent foramen ovale by transesophageal echocardiography and correlation with autopsy findings. *Am J Cardiol*. 1996;77(14):1202–9.
58. Konstadt SN, Louie EK, Black S, Rao TL, Scanlon P. Intraoperative detection of patent foramen ovale by transesophageal echocardiography. *Anesthesiology*. 1991;74(2):212–6.
59. Di Tullio M, Sacco RL, Venketasubramanian N, Sherman D, Mohr JP, Homma S. Comparison of diagnostic techniques for the detection of a patent foramen ovale in stroke patients. *Stroke*. 1993;24(7):1020–4.
60. Woods TD, Patel A. A critical review of patent foramen ovale detection using saline contrast echocardiography: when bubbles lie. *J Am Soc Echocardiogr*. 2006;19(2):215–22.
61. Thaler DE, Saver JL. Cryptogenic stroke and patent foramen ovale. *Curr Opin Cardiol*. 2008;23(6):537–44.
62. Smeenk FW, Postmus PE. Interatrial right-to-left shunting developing after pulmonary resection in the absence of elevated right-sided heart pressures. Review of the literature. *Chest*. 1993;103(2):528–31.
63. Carroll JD, Dodge S, Groves BM. Percutaneous patent foramen ovale closure. *Cardiol Clin*. 2005;23(1):13–33.
64. Krasuski RA, Hart SA, Allen D, et al. Prevalence and repair of intraoperatively diagnosed patent foramen ovale and association with perioperative outcomes and long-term survival. *JAMA*. 2009;302(3):290–7.
65. Cypel M, Yeung JC, Hirayama S, et al. Technique for prolonged normothermic ex vivo lung perfusion. *J Heart Lung Transplant*. 2008;27(12):1319–25.
66. Cypel M, Sato M, Yildirim E, et al. Initial experience with lung donation after cardiocirculatory death in Canada. *J Heart Lung Transplant*. 2009;28(8):753–8.
67. Gorcsan III J, Edwards TD, Ziady GM, Katz WE, Griffith BP. Transesophageal echocardiography to evaluate patients with severe pulmonary hypertension for lung transplantation. *Ann Thorac Surg*. 1995;59(3):717–22.
68. Izbicki G, Ben-Dor I, Shitrit D, et al. The prevalence of coronary artery disease in end-stage pulmonary disease: is pulmonary fibrosis a risk factor? *Respir Med*. 2009;103(9):1346–9.
69. Jackson A, Cropper J, Pye R, Junius F, Malouf M, Glanville A. Use of extracorporeal membrane oxygenation as a bridge to primary lung transplant: 3 consecutive, successful cases and a review of the literature. *J Heart Lung Transplant*. 2008;27(3):348–52.
70. Strueber M. Extracorporeal support as a bridge to lung transplantation. *Curr Opin Crit Care*. 2009;15(1):52–8.
71. Ebert EC. Esophageal disease in scleroderma. *J Clin Gastroenterol*. 2006;40(9):769–75.
72. Della Rocca G, Brondani A, Costa MG. Intraoperative hemodynamic monitoring during organ transplantation: what is new? *Curr Opin Organ Transplant*. 2009;14(3):291–6.
73. Marasco SF, Lukas G, McDonald M, McMillan J, Ihle B. Review of ECMO (extra corporeal membrane oxygenation) support in critically ill adult patients. *Heart Lung Circ*. 2008; 17 Suppl 4:S41–7.
74. Gammie JS, Cheul Lee J, Pham SM, et al. Cardiopulmonary bypass is associated with early allograft dysfunction but not death after double-lung transplantation. *J Thorac Cardiovasc Surg*. 1998;115(5):990–7.
75. Paradela M, Gonzalez D, Parente I, et al. Surgical risk factors associated with lung transplantation. *Transplant Proc*. 2009; 41(6):2218–20.
76. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: II. Pathophysiology, clinical importance, and management. *Anesth Analg*. 2009;108(2):422–33.
77. Subramaniam K, Yared JP. Management of pulmonary hypertension in the operating room. *Semin Cardiothorac Vasc Anesth*. 2007;11(2):119–36.
78. Murtha W, Guenther C. Dynamic left ventricular outflow tract obstruction complicating bilateral lung transplantation. *Anesth Analg*. 2002;94(3):558–9. table of contents.
79. Granton J, Moric J. Pulmonary vasodilators – treating the right ventricle. *Anesthesiol Clin*. 2008;26(2):337–53. vii.
80. Katz WE, Gasior TA, Quinlan JJ, et al. Immediate effects of lung transplantation on right ventricular morphology and function in patients with variable degrees of pulmonary hypertension. *J Am Coll Cardiol*. 1996;27(2):384–91.
81. Hausmann D, Daniel WG, Mugge A, et al. Imaging of pulmonary artery and vein anastomoses by transesophageal echocardiography after lung transplantation. *Circulation*. 1992;86 (5 Suppl):II251–8.

82. Reeves ST, Glas KE, Eltzschig H, et al. Guidelines for performing a comprehensive epicardial echocardiography examination: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr.* 2007;20(4):427–37.
83. Gonzalez-Fernandez C, Gonzalez-Castro A, Rodriguez-Borregan JC, et al. Pulmonary venous obstruction after lung transplantation. Diagnostic advantages of transesophageal echocardiography. *Clin Transplant.* 2009;23(6):975–80.
84. Michel-Cherqui M, Brusset A, Liu N, et al. Intraoperative transesophageal echocardiographic assessment of vascular anastomoses in lung transplantation. A report on 18 cases. *Chest.* 1997;111(5):1229–35.
85. Schulman LL, Anandarangam T, Leibowitz DW, et al. Four-year prospective study of pulmonary venous thrombosis after lung transplantation. *J Am Soc Echocardiogr.* 2001;14(8):806–12.
86. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation.* 2009;119(14):e391–479.
87. Jacobsohn E, Avidan MS, Hantler CB, Rosemeier F, De Wet CJ. Case report: inferior vena-cava right atrial anastomotic stenosis after bicaval orthotopic heart transplantation. *Can J Anaesth.* 2006;53(10):1039–43.
88. Rosenberger P, Shernan SK, Mihaljevic T, Eltzschig HK. Transesophageal echocardiography for detecting extrapulmonary thrombi during pulmonary embolectomy. *Ann Thorac Surg.* 2004;78(3):862–6. Discussion 866.
89. Comess KA, DeRook FA, Russell ML, Tognazzi-Evans TA, Beach KW. The incidence of pulmonary embolism in unexplained sudden cardiac arrest with pulseless electrical activity. *Am J Med.* 2000;109(5):351–6.
90. Aklog L, Williams CS, Byrne JG, Goldhaber SZ. Acute pulmonary embolectomy: a contemporary approach. *Circulation.* 2002;105(12):1416–9.
91. Thistlethwaite PA, Kaneko K, Madani MM, Jamieson SW. Technique and outcomes of pulmonary endarterectomy surgery. *Ann Thorac Cardiovasc Surg.* 2008;14(5):274–82.
92. Lengyel M. The role of transesophageal echocardiography in the management of patients with acute and chronic pulmonary thromboembolism. *Echocardiography.* 1995;12(4):359–66.
93. Chartier L, Bera J, Delomez M, et al. Free-floating thrombi in the right heart: diagnosis, management, and prognostic indexes in 38 consecutive patients. *Circulation.* 1999;99(21): 2779–83.
94. Ribeiro A, Lindmarker P, Juhlin-Dannfelt A, Johnsson H, Jorfeldt L. Echocardiography Doppler in pulmonary embolism: right ventricular dysfunction as a predictor of mortality rate. *Am Heart J.* 1997;134(3):479–87.
95. Konstantinides S, Geibel A, Kasper W, Olschewski M, Blumel L, Just H. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. *Circulation.* 1998;97(19):1946–51.
96. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr.* 2003;16(7):777–802.
97. D'Armini AM, Zanotti G, Ghio S, et al. Reverse right ventricular remodeling after pulmonary endarterectomy. *J Thorac Cardiovasc Surg.* 2007;133(1):162–8.
98. Brooker RF, Zvara DA, Roitstein A. Mediastinal mass diagnosed with intraoperative transesophageal echocardiography. *J Cardiothorac Vasc Anesth.* 2007;21(2):257–8.
99. Lin CM, Hsu JC. Anterior mediastinal tumour identified by intraoperative transesophageal echocardiography. *Can J Anaesth.* 2001;48(1):78–80.
100. Tsutsui JM, Hueb WA, Nascimento SA, Borges Leal SM, de Andrade JL, Mathias Jr W. Detection of retained surgical sponge by transthoracic and transesophageal echocardiography. *J Am Soc Echocardiogr.* 2003;16(11):1191–3.
101. Shah A, Tunick PA, Greaney E, Pfeffer RD, Kronzon I. Diagnosis of esophageal carcinoma because of findings on transesophageal echocardiography. *J Am Soc Echocardiogr.* 2001;14(11):1134–6.
102. Redford DT, Kim AS, Barber BJ, Copeland JG. Transesophageal echocardiography for the intraoperative evaluation of a large anterior mediastinal mass. *Anesth Analg.* 2006;103(3):578–9.
103. DeBoer DA, Margolis ML, Livornese D, Bell KA, Livolsi VA, Bavaria JE. Pulmonary venous aneurysm presenting as a middle mediastinal mass. *Ann Thorac Surg.* 1996;61(4):1261–2.
104. Schroder C, Schonhofer B, Vogel B. Transesophageal echocardiographic determination of aortic invasion by lung cancer. *Chest.* 2005;127(2):438–42.

21

Intra-Operative Ventilation Strategies for Thoracic Surgery

Denham S. Ward

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Key Points

- Ventilatory strategies for one-lung ventilation (OLV) should take into account preventing both intra-operative hypoxemia and postoperative ventilator-induced lung injury (VILI).
- Although a lung-protective strategy utilizing low tidal volumes (6 mL/kg) and limited inflation pressures (<30 cm H₂O) are clearly indicated for patients with acute respiratory distress syndrome, the evidence for the use of low tidal volumes for OLV is not as compelling.
- However, it seems prudent at this time to limit tidal volumes and inflation pressures during OLV, providing high breathing frequencies or P_aCO₂ are not required.
- With appropriate use of pressure and tidal volume alarms, either pressure- or volume-controlled ventilation may be used.
- Intrinsic positive end-expiratory pressure (PEEP) is common with OLV (utilizing a double-lumen endotracheal tube) and caution is warranted when high respiratory rates (short exhalation times) are utilized. The addition of external PEEP does not consistently improve oxygenation and has not been shown to reduce the incidence of VILI.
- An “open lung” maneuver utilizing several breaths of high inspiratory and expiratory pressures may improve oxygenation, but the hemodynamic consequences of the maneuver must be considered.
- No evidence-based specific recommendations can be made for OLV, but available evidence does help the anesthesiologist select the best strategy for an individual patient and surgery.

Introduction

While not all thoracic surgery requires specialized intra-operative ventilation, techniques that ventilate only a single lung are the hallmarks of anesthesia for this type of surgery. One-lung ventilation (OLV), with the collapse of the contralateral lung, greatly facilitates surgery within the thorax. With the development of video-assisted thoracoscopic surgery, the collapse of the lung on the operative side has become a necessity. OLV during these operations must ensure adequate gas exchange (arterial oxygenation and venous carbon dioxide removal), full contralateral lung deflation, and reduction of the incidence of postoperative lung injury. This last concern has grown more important as it has become clear that prevention of ventilator-induced lung injury (VILI) is important in intensive care unit treatment of acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) (see Chaps. 10 and 42 for a discussion of the definitions and treatment of ALI and ARDS). It may not always be possible to fully achieve these three goals, and anesthesiologists’ skills are required to determine the best compromise for each individual patient.

Postthoracotomy ALI, while not common, has a high mortality rate [1]. Early studies indicated a correlation with high intra-operative fluid administration [2], but subsequent studies have not shown as strong a correlation [3]. Although the causes are multifactorial [4–6], including a possible genetic predisposition [7], recent studies have pointed to intra-operative mechanical ventilation with large tidal volumes as an important risk factor [1, 3, 8, 9]. In an observational study, Licker et al. [10] used historical controls to compare outcomes

from a protective lung ventilation protocol. The protocol resulted in a decrease of ALI from 3.7 to 0.9% ($P < 0.01$) and an odds ratio of 0.34 (95% confidence interval of 0.23–0.75) adjusted for the other significant risk factors of chronic alcohol consumption, chemo-radiation therapy, more advanced cancer stage, pneumonectomy, and increased fluid administration. Their protocol utilized pressure-controlled ventilation (PCV), increased positive end-expiratory pressure (PEEP) (6.2 ± 2.4 vs. 3.3 ± 2.1 cm H₂O) and periodic lung opening maneuvers. It resulted in a lower tidal volume, 5.3 ± 1.1 vs. 7.1 ± 1.2 mL/kg (predicted body weight [PBW]), and lower inspiratory plateau pressure, 14 ± 6 vs. 20 ± 7 cm H₂O, when compared with the historical controls before implementation of the protocol. The protocol consisted of several factors (low tidal volume, PCV, PEEP, and lung opening maneuvers) that could influence the development of VILI; each of these factors will be discussed in the following sections.

Although mechanical ventilation has been in common clinical use during anesthesia since the mid-twentieth century, modern equipment has permitted the development of new modes that improve gas exchange while minimizing VILI. OLV in the operating room most commonly uses ventilators available in the operating room rather than more sophisticated intensive care unit ventilators, although the use of other ventilators has been reported [11]. While the evidence available from physiological understanding, animal studies and clinical trials is extensive, there is still no full agreement on an optimal strategy for ventilation during thoracic surgery. While the chosen ventilation strategy clearly has an immediate effect on oxygenation, the potential for opposing effects as well as many other important patient and surgical factors have made it difficult to determine the single best ventilation mode, or even predict the best mode for an individual patient. Because there are so many options for ventilator parameters, few studies are directly comparable. The clinician needs a deep understanding of ventilation and gas exchange physiology to place the clinical and animal studies into context and to be equipped for making appropriate clinical decisions.

Physiology of Single-Lung Mechanical Ventilation (see Chap. 6 for a more complete discussion)

Although there is wide terminology describing certain “modes” of ventilation (e.g., pressure-controlled, volume-controlled, inverse I:E ratio, etc.), mechanical ventilation, in a fully paralyzed patient without any spontaneous ventilatory effort, fundamentally provides a time-varying pressure waveform at the interface between the lung and its external environment. For thoracic surgery, this is invariably at the proximal end of the endotracheal tube. The resulting movement of gas into and out of the lung depends on both this waveform and the resistance and compliance of the lung, chest wall, and endotracheal tube

(see Chap. 8 of *Nunn's Applied Respiratory Physiology* [12]). Even more germane, the flow of gas into and out of the individual gas-exchanging units depends on the relative airway resistance and alveolar compliance of each unit.

While this pressure waveform can be quite complex, obviously the key characteristic is a cyclic variation in pressure through a cycle of high (inspiration) to low (expiration). Several basic clinical measurements describe this waveform, including peak and plateau inspiratory pressure, inspiratory and expiratory times, inspiratory (tidal) volume and end-expiratory pressure. This waveform not only determines the distribution of gas in the lung, but through changes in pulmonary vascular resistance and intra-thoracic pressure, will influence regional perfusion and total cardiac output. The latter can become quite important during OLV, since the unventilated lung creates an obligate shunt and the oxygen level in the venous admixture directly determines arterial oxygenation.

While modern double-lumen endotracheal tubes and bronchial blockers, combined with the routine use of fiberoptic flexible bronchoscopy, have greatly reduced the incidence of hypoxemia during OLV [13, 14], the selection of the mechanical ventilation mode clearly still plays a role. Hypoxemia during OLV is caused by venous admixture through shunts and areas of low ventilation–perfusion ratio (V/Q) gas-exchanging units. Thus, during OLV the collapsed lung is an obligate shunt, while the dependent lung also causes a venous admixture through shunt and areas of low V/Q . This is primarily through atelectatic areas of the lung seen with general anesthesia [15], and is perhaps increased with the lateral decubitus position through the weight of the mediastinum, abdominal organs and low compliance of the chest wall in the dependent position [16]. The ventilation strategy should therefore minimize perfusion to the collapsed lung and reduce areas of low V/Q in the ventilated lung. Since gas exchange not only involves providing adequate oxygenation but also adequate removal of CO₂, the total alveolar ventilation required is determined by the desired P_aCO₂. These considerations have resulted in the classic recommendation that tidal volume for OLV not be reduced (preventing atelectasis and maintaining elimination of CO₂) and the two-lung minute ventilation be maintained, often resulting in normocapnia to moderate hypocapnia with typical tidal volumes of 10 mL/kg. In this situation, the addition of PEEP causes a decrease in cardiac output and an increase in venous admixture, Fig. 21.1 [17].

Traditionally, the avoidance and treatment of arterial hypoxemia has been the essential concern of anesthesiologists during thoracic surgery with OLV [14]. Using the classic three-compartment model of gas exchange (see Chap. 8 of *Nunn's Applied Respiratory Physiology* [12]), the determinants of arterial oxygen content are: hemoglobin concentration; hemoglobin dissociation curve (P₅₀); oxygen consumption; total cardiac output (Q) [18, 19]; inspired oxygen fraction (F_iO₂) and arterial carbon dioxide (P_aCO₂) (both of which determine the alveolar oxygen level, P_aO₂); blood flow through the unventilated lung, and unventilated (or low V/Q) areas of

the ventilated lung [14, 19]. The latter two factors are often lumped together as shunt (Q_s) or shunt fraction (Q_s/Q_t) [20]; however, when considering the effects of ventilation on arterial oxygenation during OLV, it is often better to consider the blood flow through the unventilated lung ($V/Q=0$) separately from the ventilation of the low V/Q areas of the ventilated lung, since ventilation strategy may have opposing effects on these causes of venous admixture. Changes in ventilation have both direct and indirect effects on these factors (Table 21.1).

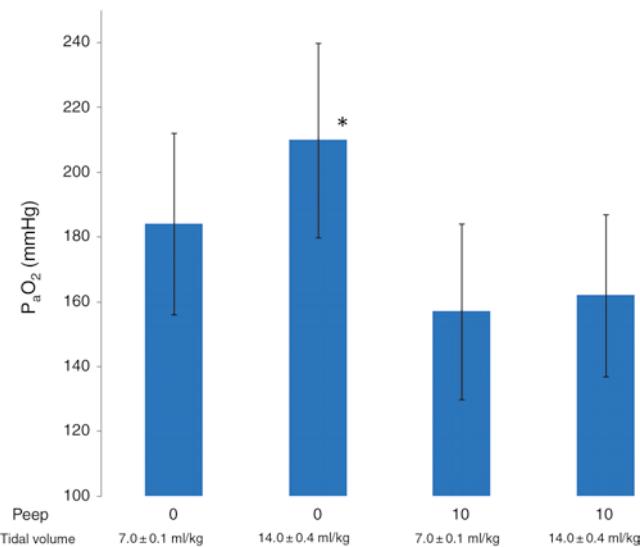


FIG. 21.1. Effect of 10 cm H₂O of positive end-expiratory pressure at tidal volumes of 8 and 16% of total lung capacity (approximately 7 and 17 mL/kg) during one-lung ventilation (OLV) (mean \pm SEM, $n=11$). Mean P_aCO_2 during all conditions was 35–38 mmHg. * $P<0.05$ different from the other conditions by two-way ANOVA. P_aO_2 arterial oxygen partial pressure; F_iO_2 fractional concentration of inspired oxygen; Q_t cardiac output; and Q_s/Q_t physiological shunt (based on data from Katz et al. [17]).

The first counter to hypoxemia during OLV is to utilize an F_iO_2 of 100%, and many anesthesiologists use 100% F_iO_2 routinely for OLV. The high-inspired oxygen concentration will reduce any residual hypoxic pulmonary vasoconstriction and increase P_AO_2 in the ventilated lung [21]. While concerns have been expressed about the absorption atelectasis caused by high F_iO_2 and the possibility of oxidative damage to the lung, neither of these factors has been explicitly studied as a possible contributor to postoperative ALI. Utilizing continuous positive airway pressure to the unventilated lung, while not possible in many procedures, e.g., video-assisted thoracotomy (VATS), this maneuver most often will ameliorate any significant hypoxemia [14, 22]. Since selection of the F_iO_2 and the use of continuous positive airway pressure are not ventilatory strategies, they will not be discussed further in this chapter.

By not decreasing total tidal volume during OLV, the distension of the ventilated lung is essentially doubled. That is, if two-lung total ventilation is typically a tidal volume of 10 mL/kg (5 mL/kg/lung) with a rate of 8–12 breaths/minute, going to OLV would be the equivalent of increasing the total tidal volume to 20 mL/kg when still ventilating two lungs. In addition, the distribution of ventilation is not uniform and is determined by regional airway resistance and alveolar compliance (see Chap. 8 of *Nunn's Applied Respiratory Physiology* [12]); thus low-resistance, high-compliance alveoli may be greatly over-distended by such high tidal volumes. The pressure–volume curve for the whole lung has an idealized sigmoid shape (Fig. 21.2). The relatively low compliance at low pressures represents the pressure needed to inflate the atelectatic collapsed portions of the lung, and the flatter, less compliant portion at high pressures represents the limits of elasticity. Tidal volumes at the lower end of the curve (no PEEP) may involve opening and closing atelectatic areas of the lung (atelec-trauma); tidal volumes at the upper end (high PEEP) may cause baro-trauma. However, Slinger et al. [23] actually measured the single-lung compliance curve and while approx-

TABLE 21.1. Effects of different ventilatory strategies on the determinants of arterial oxygenation.

Determinants of arterial oxygen content	Effect of changes in ventilation
P_{50} of the hemoglobin dissociation curve	Increased ventilation will cause a respiratory alkalosis, left shifting the curve ($\downarrow P_{50}$). While this may increase arterial saturation, unloading of oxygen in the tissue may be impaired Decreased ventilation will cause a respiratory acidosis, right shifting the curve ($\uparrow P_{50}$). While this may decrease the arterial content when the P_aO_2 is low, this may be offset by the increased ease of unloading O ₂ at the tissue (increased tissue PO ₂)
Arterial carbon dioxide (P_aCO_2)	Hyperventilation lowers the P_aCO_2 and, for a given inspired oxygen tension (F_iO_2), will increase the alveolar oxygen (P_AO_2), while hyperventilation will lower the P_AO_2 . These are relatively small effects except at the extremes of P_aCO_2
Total cardiac output (Q_t)	Increased ventilation requires a higher mean alveolar pressure which can reduce the cardiac output via a decreased venous return and increased right ventricular after-load
Blood flow through the unventilated lung (Q_s)	Increased ventilation and/or increased PEEP to dependent lung (higher mean alveolar pressure) may cause more blood to be diverted away from the ventilated lung and increase the blood flow to the unventilated lung
Blood flow through the unventilated (atelectatic or low V/Q) areas of the ventilated lung	Lower tidal volumes and/or ZEEP (zero end-expiratory pressure) may result in more atelectasis and shunt in the ventilated lung

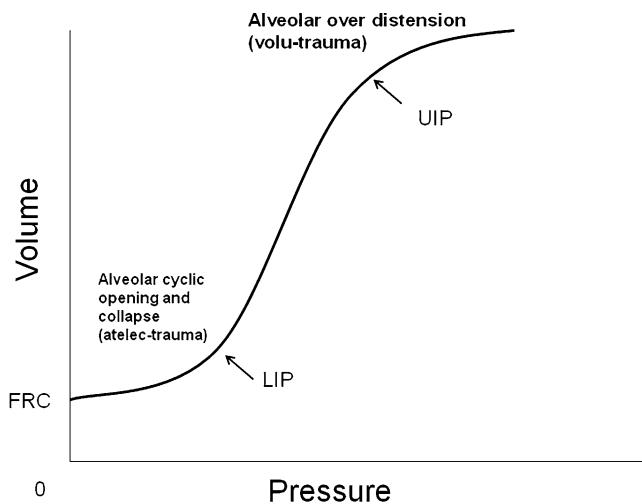


FIG. 21.2. Idealized lung pressure–volume curve. Under anesthesia, the functional residual capacity (FRC) falls too close to the residual volume, potentially causing a relatively noncompliant lung at low airway pressures as atelectatic regions of the lung are opened. At high airway pressures, the limits of distensibility may be reached. The lower inflection point (LIP) represents the pressure when the compliance increases as all atelectatic regions are opened; the upper inflection point (UIP) represents the pressure when alveoli are becoming less compliant due to overdistension.

imately a quarter of their patients did not have a lower inflection point, at volumes of 1,500 mL or a maximum pressure of 30 cm H₂O there was no decrease in compliance (no upper inflection point).

Modes of Mechanical Ventilation for OLV in the Operating Room

While modern operating room ventilators have a wide range of settings, a primary variation between ventilator types is the pressure waveform generated by a constant inspiratory *pressure* vs. a waveform generated by a constant inspiratory *flow*. These types are commonly referred to as pressure-controlled ventilators and volume-controlled ventilators. The resulting tidal volume may be the same, but the pressure and flow waveforms are quite different, although when the constant flow ventilator is used with an end-inspiratory pause, the differences in the change in lung volume with time are not as pronounced (Fig. 21.3). While not commonly used, the use of high-frequency ventilation has also been reported [11]. There are three main areas of controversy in selecting the ventilation mode for OLV: (1) pressure vs. volume ventilation; (2) high vs. low tidal volume, and (3) use of PEEP. Until recently, most studies focused on which mode would most improve oxygenation. However, the use of modern double-lumen tubes (DLTs) or bronchial blockers correctly positioned with bronchoscopic confirmation has actually greatly reduced the incidence of clinically significant hypoxemia [13]. Since the

pulse oximeter permits continuous monitoring, saturations in the high 80s are frequently well tolerated (by both the patient and the anesthesiologist) during OLV. Current research has thus focused more on the ventilator mode, primarily high vs. low tidal volume, to prevent VILI.

Pressure- vs. Volume-Controlled Ventilation

The two primary modes of ventilation commonly used in the operating room are either PCV or volume-controlled ventilation (VCV). Short-term effects of PCV or VCV on oxygenation during OLV as well as possible effects of VILI postoperatively are controversial. No definitive studies can conclusively provide specific recommendations. As can be seen from Fig. 21.3, the difference in the waveforms produced by the modes results from the decreasing airflow with PCV, when compared with the constant airflow with VCV. By adding an end-inspiratory pause to VCV, the volume trajectories of the two modes are not too dissimilar. Figure 21.4 illustrates the airway and average alveolar pressures that are generated by each of the two waveforms. The peak pressure generated by VCV for a given tidal volume is due to both airway resistance and compliance and the plateau pressure is due to the dynamic compliance (the difference between the peak and plateau pressure is determined by the airway resistance and flow). The plateau pressure for both modes is representative of the average maximum alveolar pressure and the resulting tidal volume. The mean airway pressure (the time-averaged pressure over the whole inspiratory–expiratory cycle) determines the average lung inflation.

Another way of looking at the two modes is that PCV has a high peak-inspiratory flow, which is limited in VCV, while VCV has a high peak-airway pressure that is limited in PCV. Although primarily based on animal studies, both high peak-inspiratory flows [24] and high peak-airway pressures [25] may contribute to VILI. By limiting the tidal volume and maintaining an adequate inspiratory time, both these factors can be minimized for either PCV or VCV. It is important to note that in acutely injured and inflamed lungs, the heterogeneity of the compliance, airflow resistance, and capillary blood flow of alveolar units results in a very uneven distribution of airflow, volume, and pressure throughout the respiratory cycle (Fig. 21.5). This may cause gross over-inflation (volu-trauma) of some units even though the airway pressure and total tidal volume are both limited. Both VCV with an end-inspiratory pause and PCV may permit a better distribution of the inspiration across alveolar-capillary units with different airflow time constants because of the relatively longer time at full inspiration. However, this distribution fundamentally requires an adequately long total inspiratory time. This lengthened inspiratory time may be difficult during OLV because of the conflict between the need to increase the respiratory rate (to compensate for the lower tidal volumes now recommended) and the concern about development of intrinsic PEEP as the expiratory time becomes crowded out (see next sections of this chapter).

FIG. 21.3. Pressure, flow, and volume generated by constant flow or volume-controlled ventilation (VCV) (left) and constant pressure or pressure-controlled ventilation (PCV) (right). The constant flow ventilator incorporates an end-inspiratory pause, resulting in peak and plateau pressures, while the constant pressure ventilator only has a plateau pressure. With PCV, the airflow constantly declines from the initial maximum.

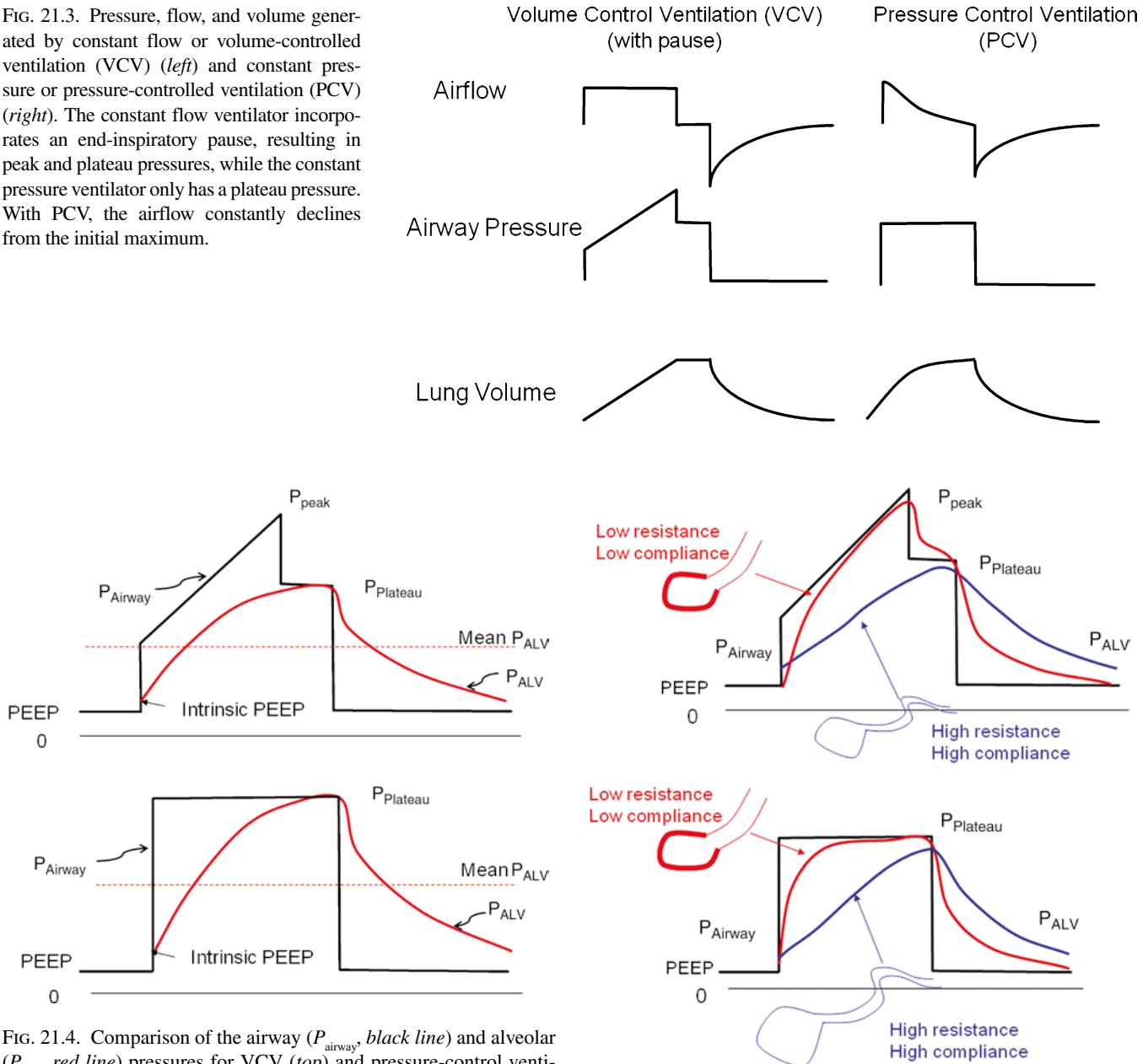


FIG. 21.4. Comparison of the airway (P_{airway} , black line) and alveolar (P_{ALV} , red line) pressures for VCV (top) and pressure-control ventilation (bottom). For VCV, both a peak (P_{peak}) and a plateau (P_{Plateau}) are observed. The difference between these pressures represents the resistance to gas flow. The PCV has only a plateau pressure.

Prella et al. [26] found that in patients with ARDS, the use of PCV permits lower peak airway pressures when tidal volumes of 9 mL/kg are used. However, no differences in blood gas values were observed. Although not commonly available in the operating room, VCV with a decreasing inspiratory flow pattern (rather than the constant inspiratory flow pattern shown in Fig. 21.3) seems to provide all the advantages of PCV but limits the possible damaging effects of the initial high peak-flow seen with PCV [27, 28].

There have been a few direct comparisons of VCV and PCV in laparoscopic surgery [29, 30] and in thoracic surgery

FIG. 21.5. The distribution of inspiratory pressure to different areas of the lung with different time constants for VCV (top) and PCV (bottom).

[31–34]. In general, these studies have shown either no or only small improvement in oxygenation with PCV over VCV. All studies for OLV used relatively large tidal volumes (9–10 mL/kg) with resulting normocapnia to mild hypocapnia. Among the four studies, only Tugrul et al. [34] showed a significant statistical improvement in P_{aO_2} , and that improvement was not clinically significant since the average S_{aO_2} was above 98% with either mode. All studies used a 10% inspiratory pause during VCV. The addition of an end-inspiratory pause in this type of ventilation can help with distribution of the

inspired gas and improve oxygenation, but, particularly in patients with chronic obstructive pulmonary disease undergoing OLV, a reduction in expiratory time to accommodate the end-inspiratory pause may increase intrinsic PEEP and reduce oxygenation [35]. No clinical studies have looked at PCV vs. VCV for prevention of postthoracotomy lung injury.

Monitoring for changes in airway pressure for VCV and in tidal volume for PCV can provide important early warning indicators of a malpositioned DLT. A possible advantage of PCV is that the tidal volume alarms can be set for increases or decreases from the current tidal volume. An increase in resistance or compliance (e.g., a left-sided DLT migrating into the left lower lobe during left lung ventilation) would cause a decrease in the delivered volume (for the set pressure) and would thereby sound the low-volume alarm. Alternately, a leak from the left side to right (e.g., from a leak around the bronchial cuff into the left lung when ventilating the right lung with a left DLT) would cause an increase in the delivered volume (but often a decrease in the returned volume, resulting in the bellows of the ventilator not completely filling if the fresh gas flow is low enough). For VCV, the airway pressure would increase if the left-sided DLT migrated into the left lower lobe orifice, but for a partial leak only the loss of the full return volume would cause an alarm. Whichever mode is used, the anesthesiologist should carefully set the appropriate alarms close to the volume currently being delivered, and understand the likely causes for any alarm activation. A timely response to an alarm, by repositioning the DLT under bronchoscopic guidance, can often prevent desaturation or unwanted inflation of the operative lung.

High vs. Low Tidal Volume

In a patient with ARDS, there is strong evidence that a lung-protective strategy improves outcomes [36–38] although Putensen et al. [39] have pointed out that there are still only a limited number of randomized controlled trials. This lung-protective strategy may include tidal volume of 6 mL/kg and plateau pressure below 25–30 cm H₂O, with the respiratory frequency adjusted to maintain CO₂ elimination (normocapnia to mild hypercapnia) and PEEP as needed to improve oxygenation without increasing the plateau pressure above 30 cm H₂O. This ventilation strategy is intended to prevent both the cyclic opening and closing of collapsed alveoli at the start of inspiration (atelectrauma) as well as the overdistension (barotrauma) of some alveoli at the end of inspiration (Fig. 21.5) [40, 41]. The mild to moderate hypercapnia and respiratory acidosis induced by this strategy are not thought to be harmful [42, 43], and may even have some beneficial effects [44]. The basic mechanisms for low tidal volumes providing protection are not entirely known, but the prevention of the induction of a pulmonary and systemic inflammatory response seems to be the common pathway [25, 45–47]. Of interest, there is increasing evidence that a further reduction in tidal volume

may be beneficial even when the P_{peak} is less than 30 cm H₂O [48] and a significant hypercapnia can be tolerated.

One point does need clarification and that is whether the tidal volume is expressed as mL per actual or per PBW. Since lung volume is more closely related to height than body weight, using actual body weight may result in particularly large tidal volumes in short, obese individuals. It is better to set the tidal volume on the basis of PBW. PBW is calculated in males: PBW (kg)=50+2.3 (height (in) –60); and in females: PBW (kg)=45.5+2.3 (height (in) –60) [49].

Although the anesthesiologist may be more concerned about acute intra-operative hypoxemia [14], the not infrequent rate of ARDS or ALI following thoracic surgery [3, 4, 9, 50, 51] has brought into focus the question of using a protective lung strategy during OLV [52]. While the use of such a strategy during OLV is currently controversial [53, 54], a recent large observational study [10] and other smaller clinical studies examining risk factors for ALI following OLV [3, 9] support the use of such a protective strategy. Fernández-Pérez et al. found an odds ratio for postoperative respiratory failure after pneumonectomy of 1.56 (95% confidence interval of 1.12–2.23) per each mL/kg of PBW (Fig. 21.6). However, the use of lower tidal volumes during anesthesia has been implicated in the development of intra-operative atelectasis which may contribute to both intra-operative hypoxemia and postoperative lung injury [55].

The role of tidal volume in influencing the development of lung or systemic inflammatory markers in patients without ALI undergoing short-term mechanical ventilation has been investigated in several studies, with some finding a correlation [56, 57] but others not finding that high tidal volumes had a pro-inflammatory effect [58]. In addition, other factors may also play a role in the development of inflammatory markers

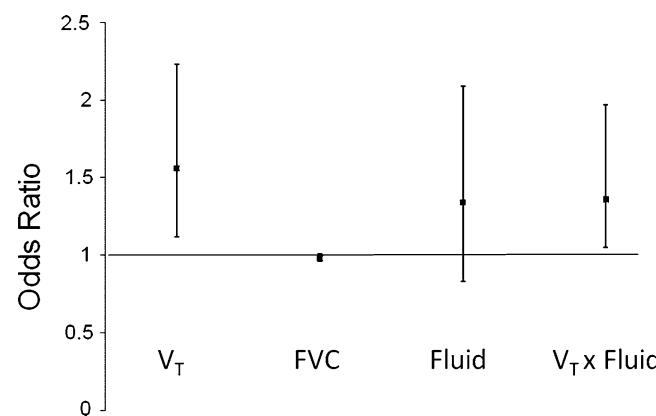


FIG. 21.6. Risk factors associated with postpneumonectomy acute lung injury. Odds ratio and 95% confidence interval from multivariate logistic regression analysis: V_T (tidal volume) is per each mL/kg predicted body weight; FVC (forced vital capacity) is for each percent decline; fluid is for each liter of fluid infused intra-operatively; and $V_T \times$ fluid is the cross-product in the logistic regression model (based on data from Fernández-Pérez et al. [3]).

following OLV, including genetics [59], the length of time of OLV [60, 61], and the patient's capacity to handle an oxidative stress [62].

The recommendations for low tidal volumes even in patients without ALI [63, 64] are based on the observed synergistic effects of high tidal volume with other lung injuries that might by themselves be subclinical ("two hit" hypothesis) [65]. This is clearest in situations where the second lung injury occurs during high tidal volume ventilation in previously healthy lungs or in a patient with developing ALI [63]. It is not as clear if the same synergism applies when the nonprotective ventilation occurs for a short period of time (intra-operative) and precedes rather than is concurrent with a second event that could cause lung injury.

Until there is a definite prospective clinical trial of sufficient size to decide the question, several factors must be considered when deciding the best strategy to use. First, as noted previously, OLV requires relatively high tidal volumes to a single lung to ensure even normocapnia to moderate hypercapnia. The recommended protective lung ventilation of 6 mL/kg is only 3 mL/kg/lung. Thus, with two-lung ventilation, 6 mL/kg may require a frequency of 12–16 breaths/min to maintain moderate hypercapnia (P_aCO_2 40–55 mmHg); initiating OLV and maintaining the 3 mL/kg/lung tidal volume may require a frequency of over 20 breaths/min and still may result in excessive hypercapnia. This rapid rate, together with the high-resistance DLT, may not permit adequate exhale time and

excessive intrinsic positive end-expiratory pressure (PEEPi) may occur [66].

Positive End-Expiratory Pressure

The use of PEEP is a mainstay for increasing oxygenation in patients with ARDS or ALI. It can also be useful in preventing cyclic opening and closing of atelectatic areas of the lung (see Figs. 21.2 and 21.7), thus potentially reducing VILI in these patients. By increasing the functional residual capacity, PEEP can prevent the closure of alveoli at the end of expiration and accomplish both an increase in oxygenation and a reduction of VILI. However, the optimal level of PEEP for both objectives is still controversial [67]. The ARDS Clinical Trials Network investigators found no difference in outcomes in patients with ARDS with either low PEEP (8.3 ± 3.2 cm H₂O) or higher PEEP (13.2 ± 3.5 cm H₂O) adjusted to maintain oxygenation [68]; subsequent studies have confirmed this finding [69, 70]. However, there is still no clear means of determining the "optimal" PEEP in ARDS/ALI [67], and there may even be subgroups that would particularly benefit from a higher level of PEEP (while maintaining the peak airway pressure below 30 cm H₂O) [71].

The factors considered for selecting PEEP for the ventilated lung in OLV differ from the factors determining PEEP in ARDS/ALI patients. First is the level of intrinsic PEEPi that is already present; second is the fact that the presence of the

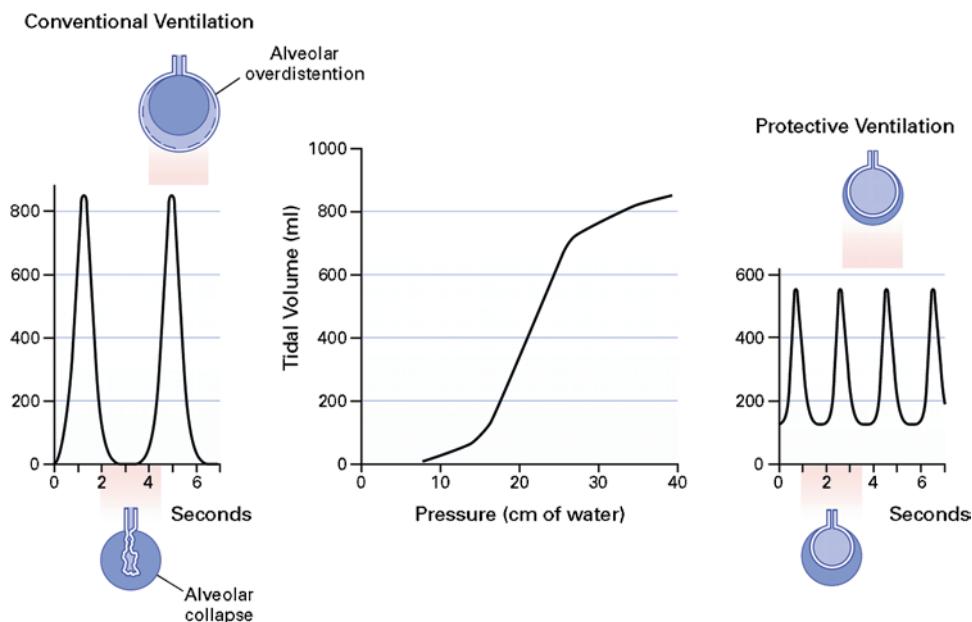


FIG. 21.7. The pressure–volume curve shown in the *middle* represents the compliance curve of a patient with acute respiratory distress syndrome. At low volumes, compliance is increased because of alveolar collapse, and at high volumes it is decreased because of overdistension. In the illustration, these inflection points occur at 14 and 26 cm H₂O, respectively. With conventional high tidal volume (12 mL/kg) and no PEEP, alveoli collapse and are overdistended on every breath (*left*). With low tidal volumes (6 mL/kg) plus PEEP (LIP plus 2 cm H₂O), the tidal volume range stays in the nondistended, noncollapsed region (*right*). Note the increase in respiratory frequency with low tidal volume to maintain CO₂ elimination (reprinted with permission from Tobin [40]. © 2001 Massachusetts Medical Society. All rights reserved).

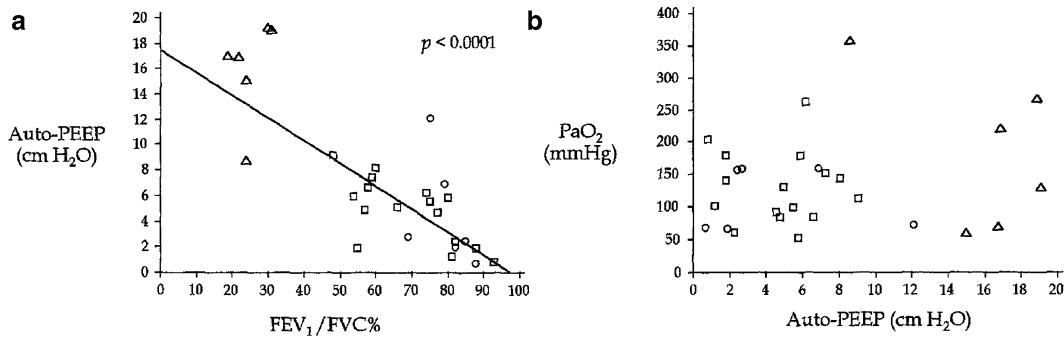


FIG. 21.8. The amount of intrinsic positive end-expiratory pressure (Auto-PEEP) was measured in patients with moderate or no obstructive lung disease (open circle), severe emphysema (open triangle) or severe fibrotic lung disease (open square) during OLV with tidal volumes of 10 mL/kg and respiratory rates of 10–12. The amount of PEEP_i was inversely related to FEV₁/FVC% (a). P_aO₂ was not correlated with PEEP_i (b) (reprinted from Ducros et al. [74]. © 1999 with permission from Elsevier).

large shunt fraction in OLV is due to the blocked ventilation to the nondependent lung rather than to the heterogeneous lung injury in ARDS. Intrinsic PEEP results from incomplete emptying of the lung back to its passive recoil equilibrium by the start of the next inspiration (end exhale) and can result from factors related both to the patient (lung resistance and compliance) and to the mechanical ventilation (endotracheal tube expiratory resistance, tidal volume, and exhale time). Patients undergoing thoracic surgery with OLV are at risk for developing PEEPi (Fig. 21.8a) [72, 73]. However, the magnitude of PEEPi is not correlated with P_aO₂ during OLV (Fig. 21.8b) [72, 74]. It is important to remember that the magnitude of PEEPi is not indicated on the usual airway pressure manometer, but requires a special maneuver to determine its presence [75, 76]. Additional factors to be considered include the relationship between PEEP and total cardiac output, and relative blood flow between the ventilated and unventilated lungs. As PEEP is increased, the average alveolar pressure increases and causes compression of the pulmonary vasculature, increasing the pulmonary vascular resistance in the ventilated lung. This increased resistance may cause more blood to flow to the nonventilated lung, resulting in a greater venous admixture. In addition, the increased after-load on the right heart and increased intra-thoracic pressure may decrease total cardiac output and reduce the mixed venous oxygen hemoglobin saturation, also resulting in an increased venous admixture. These negative effects of PEEP are countered by the improved oxygenation of the ventilated lung by assuring more open alveoli. It is not surprising that clinical studies of the effects of PEEP on arterial oxygenation during OLV have shown conflicting results [23, 77].

Early studies of the best ventilatory pattern during OLV indicated that external PEEP tended to decrease P_aO₂; in these studies, the best ventilatory strategy was for relatively large tidal volumes and no PEEP to the ventilated lung (Fig. 21.1) [17] unless continuous positive airway pressure with oxygen was applied to the unventilated lung [22]. More recent studies have generally confirmed this finding [78, 79], although

there may be sub-groups in which PEEP will improve oxygenation [80, 81].

Since PEEPi is so common in OLV, it is important to understand the complex relationship between external PEEP and PEEPi: actual total PEEP is different from applied, measured PEEP, depending on preexisting PEEPi [66]. The interaction between applied PEEP and PEEPi is not straightforward, although it is apparent from the study by Slinger and Hickey [66] that total PEEP does not increase greatly beyond PEEPi until the added PEEP approaches the value of PEEPi. It has been suggested that applying an external PEEP equal to PEEPi results in the best oxygenation [82] but PEEPi is not readily measurable in the operating room. Slinger et al. clarified the effects of PEEP on oxygenation in a study measuring the static lung compliance curve [23]. By measuring the static compliance curve, the lower inflection point (Fig. 21.2) could be identified. Without the application of external PEEP, the lower inflection point was 4.5 ± 3.5 cm H₂O, but no lower inflection point could be identified in 24% of the 42 patients studied. The value of the lower inflection point was not significantly changed by the addition of 5 cm H₂O of external PEEP. When patients were ventilated with a tidal volume of 10 mL/kg at a rate of 10 breaths/min, the measured PEEPi was 4.2 ± 3.4 cm H₂O, and the total PEEP with 5 cm H₂O added externally was 6.8 ± 1.8 cm H₂O.

Overall, no significant improvement in oxygenation was observed with the addition of PEEP. However, improvements in oxygenation were seen when total PEEP was closest to the lower inflection point. Thus, external PEEP improved oxygenation depending on the relationship between the lower inflection point, intrinsic PEEP, and total PEEP at the time external PEEP was added. The minority of patients benefiting from external PEEP had a larger lower inflection point pressure and had good elastic recoil. Presumably this good recoil resulted in an end-expiratory lung volume in the dependent lung during OLV below the normal functional residual capacity with resulting atelectasis and increased vascular resistance.

Open-Lung Procedures

Atelectasis commonly occurs even in healthy lungs under general anesthesia, and the cyclic opening and closing of atelectatic areas of the lungs (Fig. 21.7) during mechanical ventilation may contribute to VILI (atelec-trauma) [55]. Even with a protective lung ventilation strategy, it may be necessary to periodically apply higher pressures, on both inspiration and end-expiration, to open atelectatic areas of the lung [83]. Such maneuvers are often called “alveolar recruitment” or “open lung” maneuvers [83]. While such a strategy may improve oxygenation in the heterogeneously inflamed lung of ARDS, there may not be any decrease in mortality when combined with established low-tidal volume protective lung ventilation [69, 84].

The use of an open-lung procedure during OLV has been proposed, not to reduce VILI by prevention of atelec-trauma, but rather to prevent or treat intra-operative hypoxemia. As with the use of PEEP, in OLV the open-lung procedure in a noninflamed lung is quite different from its use in ARDS or ALI. However, areas of atelectasis in the dependent lung may benefit from a lung-opening procedure. While the details of the procedure vary somewhat, in essence it consists of several breaths (often 6–10) at an inspiratory pressure of 40 cm H₂O and a PEEP of 20 cm H₂O. There is also a several-breath “ramp-up” to these high pressures. Tusman et al. [85] found that such a lung recruitment procedure, when combined with a tidal volume of 6 mL/kg (peak pressures less than 30 cm H₂O), respiratory rate of 15–18, and a PEEP of 8 cm H₂O, significantly increased P_aO₂ (see Chap. 6, Fig. 6.8). Subsequently, Cinnella et al. studied the physiological effects of a lung recruitment procedure during OLV with a tidal volume of 8 mL/kg and a respiratory rate of 12, and found a similar lasting increase in P_aO₂ [86]. They also noted a decrease in cardiac output and mean arterial pressure during the maneuver, but the hemodynamic variables returned to baseline following the maneuver.

Conclusion

Anesthesiologists have many options to consider in determining the intra-operative ventilation and there is no definite evidence supporting a single strategy to prevent both intra-operative hypoxemia and postoperative ALI. A reasonable strategy would be to maintain end-inspiratory plateau pressures no greater than 30 cm H₂O, preferably less than 25 cm H₂O. To do so, tidal volume should be reduced to a range of 5–8 mL/kg of PBW during OLV, and respiratory rate increased to maintain normocapnia to moderate hypercapnia (P_aCO₂ in a range of 40–50 mmHg). Using the measured P_aCO₂ (the P_{ET}CO₂ can be used as a guide, but there is often a significant gradient between the two) greatly facilitates the adjustment of the ventilator, but an initial ventilator setting should be based on ideal or PBW, since lung volume is more

closely related to height than to actual weight [54]. Caution is warranted if the respiratory rate must be increased above the mid-teens, since excessive PEEPi may develop, causing a reduced cardiac output and hypoxemia. The initial use of low to moderate PEEP (4–8 cm H₂O) is probably unnecessary to maintain adequate oxygenation, but the use of low PEEP (5 cm H₂O) is often used to prevent atelec-trauma. However, the actual total PEEP may not change significantly with the addition of low external PEEP because of the probable existence of PEEPi during OLV. Either PCV or VCV can be used, as long as proper monitoring for changes in airway pressure and tidal volume is maintained. This ventilation strategy should prevent intra-operative hypoxemia in most patients, and may even reduce the incidence of postoperative VILI, particularly in high-risk situations (e.g., pneumonectomy, patients with a history of alcohol abuse, large intra-operative fluid requirements, men over 60 years old, longer OLV, fresh frozen plasma administration, and/or preexisting ALI). If intra-operative hypoxemia develops, then careful adjustment of PEEP and a lung-opening maneuver can be tried. Of course, correct positioning of the DLT or bronchial blocker must be verified whenever there is hypoxemia during OLV, and continuous positive airway pressure with oxygen to the unventilated lung may be successful if compatible with the surgical procedure.

Clinical Case Discussion

A 59-year-old man, weight=151 kg, height=180 cm (BMI=46.4, PBW=75.3 kg) and with a 60 pack-year smoking history (stopped smoking 2 years ago) presents for right upper lobectomy for small cell carcinoma via a right VATS. Past medical history includes hypertension and obstructive sleep apnea (CPAP at 16 cm H₂O nightly).

Preoperative pulmonary function testing showed:

FVC=2.82 L (57% predicted).

FEV₁=1.58 (42% predicted).

FEV₁/FVC=56%.

DLCO=23.9 mL/min/mmHg (79% predicted).

A left 41 French DLT was placed without difficulty and its correct position was confirmed via fiberoptic bronchoscopy. Two-lung ventilation was initiated while the patient was supine with VCV incorporating a 10% end-inspiratory pause with a tidal volume of 750 mL and a rate of 10 breaths/min. Peak airway pressures were 20 cm H₂O and the P_{ET}CO₂ was 41 mmHg. SpO₂=99% on 100% oxygen.

(a) What mode of ventilation and inspiratory gas concentration would you use for initiating OLV? What tidal volume would you use?

Either PCV or VCV would be acceptable. Initial tidal volume should be set based on the PBW, typically at 4–6 mL/kg. 6 mL/kg×75.3 kg PBW=450 mL, so initial

tidal volume should be reduced and the OLV peak and plateau pressures noted.

- (b) After setting the tidal volume to 450 mL with a rate of 14 and zero end-expiratory pressure (ZEEP), the peak inspiratory pressure was 29 cm H₂O and the P_{ET}CO₂ was 42 mmHg. Is any further adjustment of the ventilator required? Would other clinical measurements be useful?

With the peak inspiratory pressure less than 30 mmHg (presumable if VCV is being used, the plateau pressure, which is more reflective of the alveolar distending pressure, will be less than the peak) and the end-tidal CO₂ at an acceptable level, no further adjustments are needed. Initially observing the end-tidal CO₂ (P_{ET}CO₂) can guide the respiratory rate setting but a blood gas would be helpful because the increased alveolar dead space associated with this patient's COPD may result in a significant arterial to end-tidal gradient.

- (c) What would your recommendation for PEEP be after making these adjustments?

At low tidal volumes and in patients with ALI, PEEP may help reduce the opening and closing of atelectatic regions of the lung, improving oxygenation and possibly prevent further lung injury. However, PEEP may also reduce oxygenation during OLV by forcing more blood flow to the unventilated lung. PEEP up to 5 cm H₂O may be used but higher levels should be instituted cautiously.

- (d) Thirty minutes after the start of OLV, S_pO₂ falls to 88%. What maneuvers could be employed to stabilize the S_pO₂?

Whenever there is an acute decrease in the S_pO₂, the position of the DLT must be carefully checked with a fiberoptic bronchoscopy. In this case entry of the left bronchial lumen into the left lower lobe orifice would result in a significant increase in the shunt fraction.

If hypoxemia still persists after optimal positioning of the DLT, then CPAP to the unventilated lung is the most reliable way of decreasing the venous admixture, however, this is unlikely to provide acceptable operating conditions for a VATS. Switching to PCV or increasing the end-inspiratory pause with VCV may be useful. With a large DLT and a respiratory rate of only 14, then significant intrinsic PEEP is unlikely, but a reduction in the inspiratory rate (with perhaps an increase in the tidal volume) can be tried.

An "open lung procedure" with a few breaths of high PEEP and inspiratory pressure may also be of benefit, but caution must be exercised if there is any indication of hemodynamic instability.

A blood gas should be obtained and the surgeon notified that it may be necessary to return to two-lung ventilation intermittently if the saturation falls any lower. Since a low cardiac output will cause hypoxemia during OLV interventions to increase the cardiac output may be of value.

References

1. Slinger PD. Postpneumonectomy pulmonary edema: good news, bad news. *Anesthesiology*. 2006;105:2-5.
2. Zeldin RA, Normandin D, Landtwing D, Peters RM. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg*. 1984;87:359-65.
3. Fernández-Pérez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology*. 2006;105: 14-8.
4. Gothard J. Lung injury after thoracic surgery and one-lung ventilation. *Curr Opin Anaesthesiol*. 2006;19:5-10.
5. Baudouin SV. Lung injury after thoracotomy. *Br J Anaesth*. 2003;91:132-42.
6. Williams EA, Evans TW, Goldstraw P. Acute lung injury following lung resection: is one lung anaesthesia to blame? *Thorax*. 1996;51:114-6.
7. Gao L, Barnes KC. Recent advances in genetic predisposition to clinical acute lung injury. *Am J Physiol Lung Cell Mol Physiol*. 2009;296:L713-25.
8. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg*. 2003;97:1558-65.
9. Jeon K, Yoon JW, Suh GY, et al. Risk factors for post-pneumonectomy acute lung injury/acute respiratory distress syndrome in primary lung cancer patients. *Anaesth Intensive Care*. 2009;37:14-9.
10. Licker M, Diaper J, Villiger Y, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. *Crit Care*. 2009;13:R41.
11. den Hoed PT, Leendertse-Verloop K, Bruining HA, Bonjer HJ. Comparison of one-lung ventilation and high-frequency ventilation in thoracoscopic surgery. *Eur J Surg*. 1999;165: 1031-4.
12. Lumb AB. Nunn's applied respiratory physiology. 6th ed. Butterworth Heinemann: Elsevier; 2005.
13. Brodsky JB, Lemmens HJ. Left double-lumen tubes: clinical experience with 1,170 patients. *J Cardiothorac Vasc Anesth*. 2003;17:289-98.
14. Karzai W, Schwarzkopf K. Hypoxemia during one-lung ventilation: prediction, prevention, and treatment. *Anesthesiology*. 2009;110:1402-11.
15. Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brisimar B. Correlation of gas exchange impairment to development of atelectasis during anaesthesia and muscle paralysis. *Acta Anaesthesiol Scand*. 1986;30:183-91.
16. Larsson A, Malmkvist G, Werner O. Variations in lung volume and compliance during pulmonary surgery. *Br J Anaesth*. 1987;59:585-91.
17. Katz JA, Laverne RG, Fairley HB, Thomas AN. Pulmonary oxygen exchange during endobronchial anesthesia: effect of tidal volume and PEEP. *Anesthesiology*. 1982;56:164-71.
18. Levin AI, Coetzee JF. Arterial oxygenation during one-lung anaesthesia. *Anesth Analg*. 2005;100:12-4.
19. Levin AI, Coetzee JF, Coetzee A. Arterial oxygenation and one-lung anaesthesia. *Curr Opin Anaesthesiol*. 2008;21:28-36.
20. Takala J. Hypoxemia due to increased venous admixture: influence of cardiac output on oxygenation. *Intensive Care Med*. 2007;33:908-11.

21. Nagendran J, Stewart K, Hoskinson M, Archer SL. An anesthesiologist's guide to hypoxic pulmonary vasoconstriction: implications for managing single-lung anesthesia and atelectasis. *Curr Opin Anaesthesiol*. 2006;19:34–43.
22. Capan LM, Turndorf H, Patel C, Ramanathan S, Acinapura A, Chalon J. Optimization of arterial oxygenation during one-lung anesthesia. *Anesth Analg*. 1980;59:847–51.
23. Slinger PD, Kruger M, McRae K, Winton T. Relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung ventilation. *Anesthesiology*. 2001;95:1096–102.
24. Maeda Y, Fujino Y, Uchiyama A, Matsuura N, Mashimo T, Nishimura M. Effects of peak inspiratory flow on development of ventilator-induced lung injury in rabbits. *Anesthesiology*. 2004;101:722–8.
25. Uhlig S. Ventilation-induced lung injury and mechanotransduction: stretching it too far? *Am J Physiol Lung Cell Mol Physiol*. 2002;282:L892–6.
26. Prella M, Feihl F, Domenighetti G. Effects of short-term pressure-controlled ventilation on gas exchange, airway pressures, and gas distribution in patients with acute lung injury/ARDS: comparison with volume-controlled ventilation. *Chest*. 2002;122:1382–8.
27. Davis Jr K, Branson RD, Campbell RS, Porembka DT. Comparison of volume control and pressure control ventilation: is flow waveform the difference? *J Trauma*. 1996;41:808–14.
28. Campbell RS, Davis BR. Pressure-controlled versus volume-controlled ventilation: does it matter? *Respir Care*. 2002;47: 416–24.
29. Cadi P, Guenoun T, Journois D, Chevallier JM, Diehl JL, Safran D. Pressure-controlled ventilation improves oxygenation during laparoscopic obesity surgery compared with volume-controlled ventilation. *Br J Anaesth*. 2008;100:709–16.
30. Balick-Weber CC, Nicolas P, Hedreville-Montout M, Blanchet P, Stéphan F. Respiratory and haemodynamic effects of volume-controlled vs. pressure-controlled ventilation during laparoscopy: a cross-over study with echocardiographic assessment. *Br J Anaesth*. 2007;99:429–35.
31. Heimberg C, Winterhalter M, Strüber M, Piepenbrock S, Bund M. Pressure-controlled versus volume-controlled one-lung ventilation for MIDCAB. *Thorac Cardiovasc Surg*. 2006;54: 516–20.
32. Unzueta MC, Casas JI, Moral MV. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation for thoracic surgery. *Anesth Analg*. 2007;104:1029–33.
33. Choi YS, Shim JK, Na S, Hong SB, Hong YW, Oh YJ. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation in the prone position for robot-assisted esophagectomy. *Surg Endosc*. 2009;23:2286–91.
34. Tugrul M, Çamci E, Karadeniz H, Sentürk M, Pembeci K, Akpir K. Comparison of volume controlled with pressure controlled ventilation during one-lung anaesthesia. *Br J Anaesth*. 1997;79:306–10.
35. Bardoczky GI, d'Hollander AA, Rocmans P, Estenne M, Yernault JC. Respiratory mechanics and gas exchange during one-lung ventilation for thoracic surgery: the effects of end-inspiratory pause in stable COPD patients. *J Cardiothorac Vasc Anesth*. 1998;12:137–41.
36. Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. *N Engl J Med*. 2007;357:1113–20.
37. Petrucci N, Iacovelli W. Lung protective ventilation strategy for the acute respiratory distress syndrome. *Cochrane Database Syst Rev*. 2007;CD003844.
38. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1301–8.
39. Putensen C, Theuerkauf N, Zinserling J, Wrigge H, Pelosi P. Meta-analysis: ventilation strategies and outcomes of the acute respiratory distress syndrome and acute lung injury. *Ann Intern Med*. 2009;151:566–76.
40. Tobin MJ. Advances in mechanical ventilation. *N Engl J Med*. 2001;344:1986–96.
41. Mols G, Priebe HJ, Guttman J. Alveolar recruitment in acute lung injury. *Br J Anaesth*. 2006;96:156–66.
42. Morisaki H, Serita R, Innami Y, Kotake Y, Takeda J. Permissive hypercapnia during thoracic anaesthesia. *Acta Anaesthesiol Scand*. 1999;43:845–9.
43. Sticher J, Müller M, Scholz S, Schindler E, Hempelmann G. Controlled hypercapnia during one-lung ventilation in patients undergoing pulmonary resection. *Acta Anaesthesiol Scand*. 2001;45:842–7.
44. Broccard AFM. Respiratory acidosis and acute respiratory distress syndrome: time to trade in a bull market? *Crit Care Med*. 2006;34:229–31.
45. Vaneker M, Heunks LM, Joosten LA, et al. Mechanical ventilation induces a toll/interleukin-1 receptor domain-containing adapter-inducing interferon beta-dependent inflammatory response in healthy mice. *Anesthesiology*. 2009;111:836–43.
46. Curley GF, Kevin LG, Laffey JG. Mechanical ventilation: taking its toll on the lung. *Anesthesiology*. 2009;111:701–3.
47. Dos Santos CC, Slutsky AS. Invited review: mechanisms of ventilator-induced lung injury: a perspective. *J Appl Physiol*. 2000;89:1645–55.
48. Hager DN, Krishnan JA, Hayden DL, Brower RG. Tidal volume reduction in patients with acute lung injury when plateau pressures are not high. *Am J Respir Crit Care Med*. 2005;172:1241–5.
49. Predicted Body Weight Calculator. <http://www.ardsnet.org/node/77460>. Accessed 18 Dec 2009.
50. Tandon S, Batchelor A, Bullock R, et al. Peri-operative risk factors for acute lung injury after elective oesophagectomy. *Br J Anaesth*. 2001;86:633–8.
51. Kutlu CA, Williams EA, Evans TW, Pastorino U, Goldstraw P. Acute lung injury and acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg*. 2000;69:376–80.
52. Lytle FT, Brown DR. Appropriate ventilatory settings for thoracic surgery: intraoperative and postoperative. *Semin Cardiothorac Vasc Anesth*. 2008;12:97–108.
53. Slinger P. Pro: low tidal volume is indicated during one-lung ventilation. *Anesth Analg*. 2006;103:268–70.
54. Gal TJ. Con: low tidal volumes are indicated during one-lung ventilation. *Anesth Analg*. 2006;103:271–3.
55. Duggan M, Kavanagh BP. Pulmonary atelectasis: a pathogenic perioperative entity. *Anesthesiology*. 2005;102:838–54.
56. Michelet P, D'Journo XB, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology*. 2006;105:911–9.
57. Schilling T, Kozian A, Huth C, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. *Anesth Analg*. 2005;101:957–65.

58. Wrigge H, Uhlig U, Zinserling J, et al. The effects of different ventilatory settings on pulmonary and systemic inflammatory responses during major surgery. *Anesth Analg*. 2004;98:775–81.
59. Shaw AD, Vaporciyan AA, Wu X, et al. Inflammatory gene polymorphisms influence risk of postoperative morbidity after lung resection. *Ann Thorac Surg*. 2005;79:1704–10.
60. Tekinbas C, Ulusoy H, Yulug E, et al. One-lung ventilation: for how long? *J Thorac Cardiovasc Surg*. 2007;134:405–10.
61. Mishos P, Katsaragakis S, Milingos N, et al. Postresectional pulmonary oxidative stress in lung cancer patients. The role of one-lung ventilation. *Eur J Cardiothorac Surg*. 2005;27:379–82.
62. Cheng YJ, Chan KC, Chien CT, Sun WZ, Lin CJ. Oxidative stress during 1-lung ventilation. *J Thorac Cardiovasc Surg*. 2006;132:513–8.
63. Gajic O, Dara SI, Mendez JL, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. *Crit Care Med*. 2004;32:1817–24.
64. Schultz MJ. Lung-protective mechanical ventilation with lower tidal volumes in patients not suffering from acute lung injury: a review of clinical studies. *Med Sci Monit*. 2008;14: RA22–6.
65. Bonetto C, Terragni P, Ranieri VM. Does high tidal volume generate ALI/ARDS in healthy lungs? *Intensive Care Med*. 2005;31:893–5.
66. Slinger PD, Hickey DR. The interaction between applied PEEP and auto-PEEP during one-lung ventilation. *J Cardiothorac Vasc Anesth*. 1998;12:133–6.
67. Levy MM. PEEP in ARDS – how much is enough? *N Engl J Med*. 2004;351:389–91.
68. Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med*. 2004;351:327–36.
69. Meade MO, Cook DJ, Guyatt GH, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299:637–45.
70. Mercat A, Richard JC, Vielle B, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299:646–55.
71. Gattinoni L, Caironi P. Refining ventilatory treatment for acute lung injury and acute respiratory distress syndrome. *JAMA*. 2008;299:691–3.
72. Yokota K, Toriumi T, Sari A, Endou S, Mihira M. Auto-positive end-expiratory pressure during one-lung ventilation using a double-lumen endobronchial tube. *Anesth Analg*. 1996;82:1007–10.
73. Bardoczky GI, Yernault JC, Engelman EE, Velghe CE, Cappello M, Hollander AA. Intrinsic positive end-expiratory pressure during one-lung ventilation for thoracic surgery. The influence of preoperative pulmonary function. *Chest*. 1996;110:180–4.
74. Ducros L, Moutafis M, Castelain MH, Liu N, Fischler M. Pulmonary air trapping during two-lung and one-lung ventilation. *J Cardiothorac Vasc Anesth*. 1999;13:35–9.
75. Blanch L, Bernabé F, Lucangelo U. Measurement of air trapping, intrinsic positive end-expiratory pressure, and dynamic hyperinflation in mechanically ventilated patients. *Respir Care*. 2005;50:110–23.
76. Bardoczky GI, d'Hollander AA, Cappello M, Yernault JC. Interrupted expiratory flow on automatically constructed flow-volume curves may determine the presence of intrinsic positive end-expiratory pressure during one-lung ventilation. *Anesth Analg*. 1998;86:880–4.
77. Benumof JL. One-lung ventilation: which lung should be PEEPed? *Anesthesiology*. 1982;56:161–3.
78. Mascotto G, Bizzarri M, Messina M, et al. Prospective, randomized, controlled evaluation of the preventive effects of positive end-expiratory pressure on patient oxygenation during one-lung ventilation. *Eur J Anaesthesiol*. 2003;20:704–10.
79. Leong LM, Chatterjee S, Gao F. The effect of positive end expiratory pressure on the respiratory profile during one-lung ventilation for thoracotomy. *Anaesthesia*. 2007;62:23–6.
80. Cohen E, Eisenkraft JB. Positive end-expiratory pressure during one-lung ventilation improves oxygenation in patients with low arterial oxygen tensions. *J Cardiothorac Vasc Anesth*. 1996;10:578–82.
81. Valenza F, Ronzoni G, Perrone L, et al. Positive end-expiratory pressure applied to the dependent lung during one-lung ventilation improves oxygenation and respiratory mechanics in patients with high FEV₁. *Eur J Anaesthesiol*. 2004;21:938–43.
82. Inomata S, Nishikawa T, Saito S, Kihara S. “Best” PEEP during one-lung ventilation. *Br J Anaesth*. 1997;78:754–6.
83. Lachmann B. Open up the lung and keep the lung open. *Intensive Care Med*. 1992;18:319–21.
84. Lapinsky SE, Mehta S. Bench-to-bedside review: recruitment and recruiting maneuvers. *Crit Care*. 2005;9:60–5.
85. Tusman G, Böhm SH, Sipmann FS, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. *Anesth Analg*. 2004;98:1604–9.
86. Cinnella G, Grasso S, Natale C, et al. Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. *Acta Anaesthesiol Scand*. 2008;52:766–75.

Anesthesia for Open Pulmonary Resection: A Systems Approach

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Key Points

- Perioperative morbidity and mortality is common following lung resection, with most deaths (>75%) attributed to major adverse pulmonary events (MAPE; including pneumonia, acute lung injury [ALI], and acute respiratory distress syndrome [ARDS]).
- Perioperative risk can be managed by dividing risk into two broad categories: iatrogenic risk and patient-attributed risk. Clinical care pathways manage iatrogenic risk, while perioperative strategies that allow identification and optimal management of high-risk patients manage patient-attributed risk. These factors will improve outcomes and reduce hospital costs.
- Patient safety and the delivery of quality care, with emphasis on systems improvement, have emerged as central tasks for healthcare providers. In fact, benchmarking of data will increasingly allow patients to identify institutions that deliver on the value proposition – providing medical care that measures up in safety and quality and yet is delivered at significantly lower costs.

General Concepts

Perioperative morbidity and mortality is common following lung resection (Table 22.1). Importantly, while the studies summarized in Table 22.1 highlight an increasing incidence of morbidity and mortality with increased volume of lung resected [1], these studies consistently report a need for improved predictors of adverse postoperative outcome.

Further, major adverse pulmonary events (MAPE; including pneumonia, acute lung injury [ALI], and acute respiratory distress syndrome [ARDS]) have a high rate of mortality and contribute singularly to most (>75%) perioperative deaths. While a decline in adverse outcome has been witnessed over the last 50 years, it is important that we continue to seek strategies to improve perioperative outcome following open lung surgery. Recent strategies that have contributed to a reduction in the incidence and the mortality associated with ALI/ARDS include surgical attempts to limit the volume of lung resected (e.g., performing a sleeve resection rather than a pneumonectomy) and protective lung ventilation strategies (tidal volume reduction proportional to the number of segments resected) [2].

Strategies to further improve surgical outcome require a global approach, with implementation of (1) clinical care pathways that reduce iatrogenic risk and (2) perioperative strategies that focus on identifying and optimally managing the high-risk patient to reduce patient-attributed risk. Clinical care paths should embrace safety and quality initiatives, which when implemented within clinical practice, should encompass improvements in reliability (reduced variability), processes, performance, and be combined with cost measures to assess the value of the care delivered. With society increasingly intent on actualizing the value proposition of healthcare, we are obligated to deliver optimized quality care within the constraints of cost [3]. Driven by the unsustainable growth in healthcare expenditure – accounting for 10–16% of the Gross Domestic Product in developed nations – the need to improve quality and reduce costs has rapidly become the mantra of the healthcare industry.

TABLE 22.1. Summary of key studies illustrating the incidence of perioperative morbidity and mortality associated with major lung resection.

Author	Year	N	Morbidity	Mortality	Factors associated with mortality	Commentary
Kopec et al.	1998		All morbidities 40–60%	Right vs. left pneumonectomy 10–12% vs. 1–3.5%	3.5%	1. Review of literature on pneumonectomy 2. Mortality has decreased significantly from 56.4% reported in www–1940
Kutlu et al.	1991–1997	1,139				1. Review of all lung resections performed at an single institution 2. While incidence of ALI/ARDS is low (3.9%) it is a leading cause of mortality 3. >75%* of mortality is associated with major adverse pulmonary events
Vaporciyan et al.	2002	257	MAPE only 12.8%	Overall mortality 6.2%	Mortality in patients without and with MAPE 2.1% vs. 39.3%	1. Single institution review of pneumonectomy 2. Smoking cessation within 1 month of surgery was only multivariate predictor of risk 3. High mortality observed in patients that suffer a major adverse pulmonary event
Dulu et al.	2002–2004	2,039	Incidence of ALI/ARDS 2.5%	Mortality associated with ALI/ARDS 40%	Incidence (and mortality) of ALI/ARDS by type of lung resection Pneumonectomy: 7.9% (50%) Lobectomy: 2.96% (42%) Segmentectomy: 0.88% (22%)	1. Review of incidence of ALI/ARDS following lung resections performed at a single institution 2. Increased incidence of ALI/ARDS with increasing lung volume resected 3. High mortality in patients that suffering ALI/ARDS
Tang et al.	1991–1997 2000–2005	1,376	Incidence of ALI/ARDS 3.2%	Mortality associated with ALI/ARDS 72%	Pneumonectomy rate = 17.4% of resections Pneumonectomy rate = 6.4% of resections 45%	1. Review of incidence of ALI/ARDS following lung resections performed at a single institution over two time periods 2. High mortality in patients that suffering ALI/ARDS 3. Reduced incidence (and associated mortality) of ALI/ARDS after 2,000 associated with two factors: a. Aggressive strategies to avoid pneumonectomy b. Lung protective ventilation strategies (reduced tidal volume per number of resected segments)

The Institute of Medicine's report on patient safety *To Err is Human: Building a Safer Health System* estimates that 100,000 people die each year from medical errors in U.S. hospitals [4]. This report, a landmark study in modern medicine, is an important contributor to the current patient-safety movement, with patient safety and the delivery of quality care emerging as central issues in medicine and as central tasks for healthcare providers in the last decade. In fact, quality healthcare is now a worldwide goal. Consequently, an important paradigm shift occurred: with (1) emphasis shifting to systems improvement rather than exhortations to individual health professionals and (2) recognition that leadership in healthcare institutions is a key catalyst in improving patient safety and in the delivery of quality care. The Institute of Medicine defines "quality" as "the degree to which health services increase the likelihood of desired health outcomes, consistent with current professional knowledge" and as such recommends six standards of care (safe, effective, patient-centered, timely, efficient, and equitable) to achieve the delivery of quality healthcare [5].

Additionally, economic factors, such as reimbursement programs, market forces, and globalization of healthcare, will continue to drive the need to deliver quality care. Hospitals will increasingly compete for patients on the grounds of quality at local, regional, and global (medical tourism) levels. In this regard, reimbursement programs, such as pay for performance (P4P) or refusal of payment for preventable "never events," will increasingly be used to link patient outcomes with reimbursement. Benchmark data will increasingly allow patients to identify institutions that deliver on the value proposition – providing medical care that measures up in safety and quality at a lower cost.

A Systems Approach

Continued improvement in patient outcome is feasible when one understands and manages the risk types found within the complexity of a patient presenting for thoracic surgery. This complexity originates in the patient's disease process and associated comorbidities (patient-attributed risk; Fig. 22.1) and within the complexity of the healthcare system (iatrogenic risk). The majority of risk is derived from the burden of disease and the comorbidities that patients present with. However, iatrogenic risk, the risk of adverse outcome associated with therapy (medical, including anesthesia, or surgical therapy, or lack thereof, imposed by a third-party, the healthcare provider), remains sizeable, with an estimated 100,000 deaths occurring each year in the U.S [4]. Importantly, this risk is largely preventable.

A strategy for understanding, examining, and improving care patterns, with the intended consequence of improved surgical outcome, and based on the two broad risk categories (iatrogenic and patient-attributed risk) is outlined in Fig. 22.2. This systems approach divides care into three broad areas based on decision points at Q1 and Q2.

PATIENT ATTRIBUTED RISK

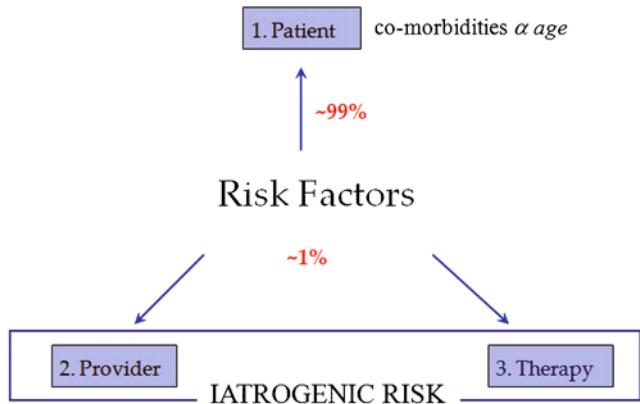


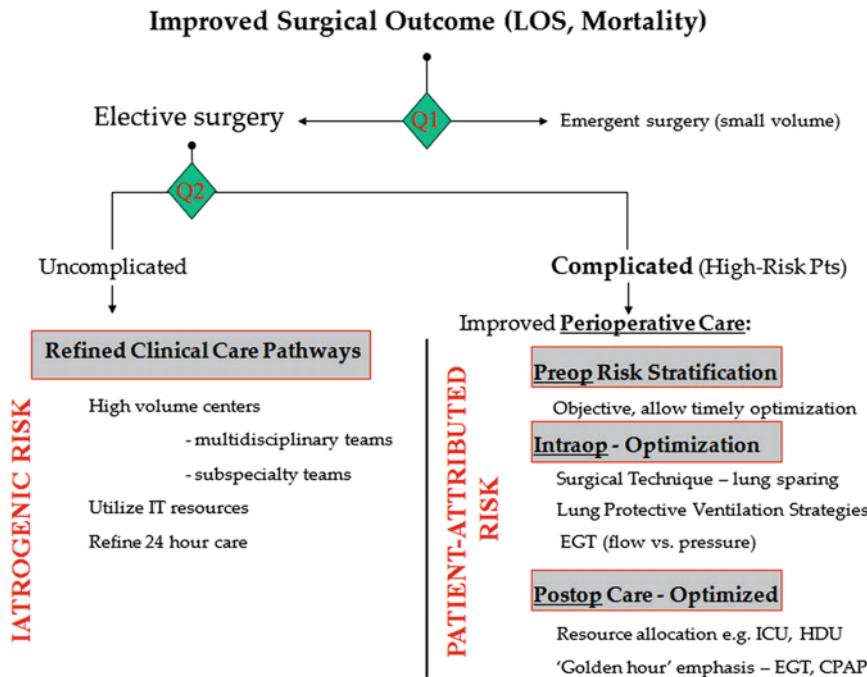
FIG. 22.1. Complexity and risk for adverse outcome originates in the patient's disease process and associated comorbidities (patient-attributed risk) and within the complexity of the healthcare system (iatrogenic risk).

Decision point Q1 delineates elective surgical care from emergent surgical care. While emergency procedures account for a small fraction of the thoracic surgical case load, these patients nevertheless are often critically ill, have limited time for preoperative optimization, and are at significant risk for a protracted and costly length of hospital stay. Decision point Q2 delineates care into processes that: (1) deliver the value proposition of the surgical procedure – delivering uncomplicated surgical outcome in a cost-effective manner through the implementation of clinical care pathways, thereby reducing iatrogenic risk; and (2) provide cost-effective perioperative risk stratification and optimization of high-risk patients – reducing patient-attributed risk and associated postoperative morbidity and mortality. The former processes are predominantly directed at the surgical disease and accompanying surgical procedure, while the latter are predominantly directed at the underlying disease burden and the medical comorbidities of the patient.

Patient Care Processes in Thoracic Anesthesia

The events involved between a patient presenting for thoracic surgery and having him/her discharged safely represent an extraordinarily complex system. This requires the collection, verification, and distribution of a large volume of information through multiple healthcare providers (including primary care physicians, pulmonologists, thoracic surgeons, oncologists, radiologists, cardiologists, nurse practitioners, and physiotherapists). Further complexity is added by the sophistication of the high acuity perioperative environment, with numerous perioperative physiological monitors and surgical instruments. A high volume of information must be processed in real time, communicated effectively throughout the operative team, and acted upon. Harm can originate at a multitude of levels. The

FIG. 22.2. A strategy for understanding, examining, and improving care patterns, with the intended consequence of improved surgical outcome. *CPAP* continuous positive airway pressure; *EGT* early goal directed therapy; *HDU* high dependency unit; *ICU* intensive care unit; *IT* information technology; *LOS* length of stay; *postop* postoperative; *Q1, Q2* decision points.



uncertainty and urgency inherent in the decision-making processes produce risk, which is compounded by external stressors, such as work load, fatigue, and a great degree of variability in organizational and/or environmental structures that support decision making and physical tasks. After completion of the surgical procedure, patients then typically reside in the post-anesthesia care unit where care decisions are divided between anesthesiologists, surgeons, and the acute pain team, all of whom have ongoing responsibilities. Even when the patient is ensconced on the hospital ward, care for chest tubes, pulmonary toilet, X-ray follow up, medication therapy, etc., require a continuous flow of interactions and communication.

Recent progress in patient safety originates from the adoption of a systems analysis approach developed in other high-risk environments such as aviation. Vincent et al. [6] (among others) adopted these approaches for patient care (Table 22.2) and further modified these specifically to suite the perioperative care of the surgical patient (Table 22.3). Improved safety evolves from the study of this exhaustive list, which covers all aspects of the patient, the patient's interactions with the care team, the interaction amongst members of the care team, and the interactions of the patient and care team with the hospital environment. This has changed the focus of care from one of a surgeon's skill vs. the patient's disease to one of care that encompasses development of the care pathways that ensure consistent best practice regardless of the care giver, individual performance within a team setting, optimal team coordination and communication, and the interaction of all of these aspects within the larger hospital organization/environment – all of which can help or hinder performance. Such approaches require a nonpunitive culture that promotes open dialog with a focus on improved patient outcomes.

TABLE 22.2. Framework of factors influencing clinical practice.

Factor types	Influencing contributory factors
Institutional context	Economic and regulatory context National health service executive Clinical negligence scheme for Trusts
Organizational and management factors	Financial resources and constraints Organizational structure Policy standards and goals Safety culture and priorities Staffing levels and skills mix Workload and shift patterns Design, availability, and maintenance of equipment
Work environment factors	Administrative and managerial support Verbal communication Written communication Supervision and seeking help Team structure (consistency, leadership, etc.)
Team factors	Knowledge and skills Competence
Individual (staff) factors	Physical and mental health
Task factors	Task design and clarity of structure Availability and use of protocols Availability and accuracy of test results
Patient factors	Condition (complexity and seriousness) Language and communication Personality and social factors

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While there have been few specific studies of a systems approach in thoracic surgery, clear examples abound. Although controversial, increasing data support benefits through reduced morbidity and improved survival in patients having high-risk operations performed by subspecialty-trained surgeons in

TABLE 22.3. Principal features of the operation profile.

Patient factors
Principal complaint
Comorbidities
ASA, BMI, age, and other relevant clinical information
The surgical team
Personnel
Experience of previous work together
Familiarity with procedure
Fatigue, sleep loss, stress, etc.
Processes and procedures
Adequacy of notes and management plan
Consent and preparation
Anesthetic procedures
Key operative events
Blood loss
Minor and major complications
Error compensation and recovery
Flow of information regarding patient
Adequacy of notes and consent
Specific intraoperative communications
Handover
Technical skills
Ratings of good general surgical practice
Ratings of operation-specific steps
Identification of specific technical errors
Team performance and leadership
Leadership
Coordination between team members
Willingness to seek advice and help
Responsiveness and flexibility
Decision-making and situation awareness
Patient limitations
Operation limitations
Surgeon's limitations
Team limitations
The operative environment
Availability and adequacy of equipment
Availability of notes, records
Noise and lighting
Distractions
Interruptions
Phone calls, messages, outside theater events, etc.

high-volume practices [7, 8]. Such results are especially evident in esophageal cancer surgery, colorectal cancer surgery, and vascular surgery [7, 9–11]. While the volume effect may speak for the technical proficiency of the surgeon, it is likely to also reflect on the wider care services provided by other team members, including anesthesiologists, intensive care physicians, nurses, physiotherapists, etc. The effect of wider care services has been demonstrated in patients requiring thoracotomy for lobectomy where defined clinical care pathways both improved outcomes and reduced hospital costs [12, 13]. These pathways have the further benefit of patient education, managing patient and family expectations, educating junior house staff and new care team members, and defining points of care and team interaction with the patient where data can be collected, analyzed, and benchmarked.

Care patterns and outcomes need to be assessed and examined both for benchmarks; to track changes from trends in technology, reimbursement, or patient issues; and to seek improvement

in outcomes. These outcomes need to be examined locally and against national data such as the General Thoracic Surgery Database – a component of the Society of Thoracic Surgeons (STS) National (U.S.) Database, which comprises, as of January 2009, data on 88,000 surgical procedures submitted by 126 participating sites. Potential biases in these data include the voluntary reporting process and the fact that most of the participating centers are affiliated with surgical training and/or research institutions – with the potential for such institutions to have sicker or more complicated patients and thus worse outcomes if the data are not appropriately adjusted for risk. Mandatory reporting, such as the National Surgical Quality Improvement Program (NSQIP) in the U.S., may provide more reliable comparative data due to wider data capture, incorporating more diverse patients, and thereby facilitate risk adjustment.

Once the care pathway has been defined and the internally collected data have been reviewed and examined against external benchmark data, meaningful changes can then be implemented. For example, as a result of the NSQIP program, the changes implemented in the U.S. Veterans Affairs hospital system decreased the 30-day morbidity from major surgery by 45% and decreased 30-day mortality by 27% [14, 15]. Such improvements promise expansion into other surgical avenues and potentially into outcomes other than morbidity and mortality that include patient and provider satisfaction with the care process [14, 15].

Preoperative Care

In the North America and Europe the majority of patients present for open thoracic procedures with a confirmed diagnosis of cancer or an intrathoracic process suspicious for cancer. In contrast, patients in the developing world are likely to present with trauma or pulmonary infection. Patients also often present with comorbidities, especially smoking-related comorbidities that dramatically increase their risk for perioperative pulmonary and cardiac complications. Irrespective of the underlying disease mechanism, all patients require a thorough preoperative assessment to address and improve correctable physiological problems and to assure adequate physiological reserve following surgical intervention. The preoperative evaluation needs to be focused on preoperative risk stratification, identification of reversible pathologies, and decreasing the patient's risk through preoperative optimization (see Chap. 2 for a detailed review). Beyond reducing risk, preoperative interaction with the patient allows practitioners to mentally prepare patients for the rigors of recovery.

Preoperative smoking cessation and pulmonary rehabilitation have not been consistently noted to be effective in improving outcomes [16, 17]. Practitioners should ensure continuation of bronchodilator therapy throughout the perioperative period. Patients need to understand the importance of complying with their pulmonary toilet; moreover, it should be explained that even with aggressive postoperative epidural analgesia combined with multimodal therapy visual analog

pain scores with pulmonary toilet are typically 5 out of 10 for the first 5 postoperative days [18].

For patients with cardiovascular comorbidities, the acute introduction of beta-blocker therapy may increase the risk for cardiovascular harm [19]. Similarly, randomized trials of coronary revascularization before major surgery have not shown any clear benefits [20–24]. As such, it is currently recommended that the preoperative evaluation of coronary artery disease should only be addressed in those patients with acute changes in symptoms, while focusing on optimized medical therapy and exploring other cardioprotective strategies (e.g., statins) for the remaining patients with stable coronary disease.

If beta-blockers are indicated for intercurrent medical conditions, then these medications should be started well before rather than at the time of surgery. In cases where coronary heart disease is only recognized at the time of admission for elective surgery, results of the POISE trial suggest that while acute perioperative administration of beta-blocker therapy may confer cardioprotection, it increases the risk of stroke and all-cause mortality [19]. Further, beta-blocked patients seem to tolerate surgical anemia less than patients who are naïve to beta-blockers, resulting in increased adverse postoperative events [25].

Studies suggest that the pleiotropic effects (nonlipid lowering effects, including antiinflammatory effects and endothelial modulation) of statins improve outcomes in the perioperative period in patients undergoing major cardiac and noncardiac surgery [26, 27]. The best evidence comes from vascular surgery patients where preoperative fluvastatin, commenced at least 30 days before (and continued for at least 30 days after surgery), significantly reduced postoperative myocardial ischemia and death from cardiovascular causes, without adverse skeletal muscle or hepatic injury. These pleiotropic effects of statin therapy may translate into perioperative protection of heart, brain, and kidney for other major surgeries, but more robust data are required. Specific to the thoracic surgery population, preoperative statin therapy is reported to result in a threefold reduction in the incidence of postoperative atrial fibrillation [28].

Antihypertensive medications (including beta-blockers), HMG Co-A reductase inhibitor (statin) therapy, and where possible antiplatelet therapy, should be continued to avoid potential cardiovascular harm associated with drug withdrawal [29–31]. Controversy, however, surrounds the preoperative management of antiplatelet therapy, with increasing data supporting the continuation of clopidogrel and aspirin in the perioperative period to reduce both stroke and myocardial infarction [32]. Factors increasing the risk for such thrombotic adverse events include poor endothelialization of drug-eluting coronary stents, hypercoagulability induced by the surgical stress response, and a rebound response from the perioperative withdrawal of antiplatelet therapy. To prevent acute in-stent thrombosis, patients with bare metal and drug-eluting coronary stents should continue dual antiplatelet therapy for a minimum of 3 and 12 months, respectively, after stent placement, with consideration for lifelong antiplatelet monotherapy; thereafter patients at increased risk may require lifelong

dual antiplatelet therapy. If possible, elective surgery should be performed beyond this 3- or 12-month window and strong consideration given to continue dual antiplatelet therapy, with a minimum of antiplatelet monotherapy with aspirin, throughout the perioperative period. This continuation protocol needs to be balanced against the risk of perioperative bleeding and the need for epidural analgesia.

Intraoperative Care

Operating room preparation needs to occur as with every case to ensure patient safety. In addition to a routine setup, typical airway management equipment includes methods of establishing (double lumen tubes [DLT], bronchial blockers, or Univent tubes) and verifying (pediatric fiberoptic bronchoscope) lung isolation. A circuit for delivering continuous positive airway pressure (CPAP) to the nondependent lung should be immediately available. Other devices that should be in the room include the following: a “bean bag” placed on the operating table prior to the patient’s arrival; an arm holder for positioning the nondependent arm; warming devices such as intravenous fluid warmers and warm air blankets for maintaining normothermia in patients and thereby negating the adverse effect of hypothermia on hypoxic pulmonary vasoconstriction (HPV), coagulopathy, and wound healing; and mechanical compression devices to prevent thromboembolism.

Once consent is obtained and the patient has been properly identified and the surgical site marked, an intravenous catheter should ideally be placed in the hand/wrist/forearm of the operative (nondependent) side. The antecubital fossa is not ideal due to the position of the arms in the lateral decubitus position where the arms will be bent at 90° and the flow potentially inhibited. An 18-gauge intravenous catheter is sufficient for medication and fluid management since a thoracotomy in a hemithorax that has not had previous surgery, chest tubes, trauma, or radiation therapy, the operative blood loss should be minimal. However, after induction of anesthesia, an additional intravenous cannula is typically placed in case of sudden unanticipated blood loss. This is especially mandatory in reoperative cases or cases that require an extrapleural approach (e.g., extrapleural pneumonectomy for mesothelioma). If surgical dissection is required around the greater veins (vena cavae or subclavian veins), contralateral access, central access, and/or lower extremity access should then be considered.

Patient safety decisions need to be incorporated into the preoperative and early operative phase. These include the following: surgical site marking, thromboembolic prophylaxis (sequential compression stockings or subcutaneous heparin), strategies to maintain normothermia, antibiotic administration within 1 h prior to incision, universal precautions (gown and gloves) as mandated for invasive procedures, and a type and screen for blood cross-matching sent to transfusion services.

Paravertebral and epidural catheter placement are equally efficacious for postoperative analgesia [33–35]. Regional anesthesia is typically established in the preoperative area or in the operating room prior to induction, with the goal of establishing

adequate analgesia prior to completion of the surgical procedure and emergence from anesthesia. Once the patient is positioned for regional anesthesia, noninvasive monitoring (pulse oximeter and blood pressure cuff) and nasal oxygen are applied, and sedation is then administered to facilitate regional anesthesia. Typical sedative regimens used to facilitate the induction of regional anesthesia include titrated doses of midazolam and/or fentanyl as dictated by patient anxiety and medical status. Dexmedetomidine is a viable alternative for sedation, especially if it is planned to be used as part of the general anesthetic technique or if awake fiberoptic bronchoscopy (usually for an anticipated difficult airway) is planned preceding the induction of general anesthesia.

After securing the regional anesthesia catheter, the patient is positioned in the supine position and the standard American Society of Anesthesiologists (ASA) monitors placed. The placement of the EKG leads requires an understanding of the surgical approach. For a thoracotomy, care should be taken to avoid trapping the electrodes and leads between the patient and the bed as this can lead to pressure necrosis. For a left-sided thoracotomy, the V₅ lead cannot be placed in its usual position over the fourth interspace in the anterior axillary line as this intrudes on the surgical field. It is typically placed in the V₁ position (second interspace, right of the sternum). These factors (modified lead placement and lateral decubitus positioning) are likely to reduce the sensitivity of such monitoring for ischemic events.

After all noninvasive monitors are secured, preoxygenation is commenced. Five minutes of tidal breathing preoxygenation compensates for delayed nitrogen washout in patients with chronic obstructive pulmonary disease (COPD) [36]. During this period, a preinduction arterial line can be placed if needed; however, in hemodynamically stable patients this is typically done after induction of anesthesia. Placement of the arterial line is typically preferred in the dependent arm to avoid waveform damping by compression of the ono-dependent wrist by the over-head arm holder.

Induction agents are chosen in relation to the patient's medical status, and are intended to blunt the sympathetic stimulation associated with laryngoscopy and intubation without producing deleterious hypotension. Propofol doses of 0.5–1 mg/kg can adequately ensure unconsciousness with minimal hemodynamic impact. Etomidate doses of 0.1–0.2 mg/kg are reasonable alternatives. A reduction in the dose of the induction agent, thereby avoiding hypotension, can be achieved by incorporating analgesic agents during induction and by ensuring that the peak effect of analgesia coincides with laryngoscopy. The onset of significant analgesia following intravenous fentanyl, sufentanil, and remifentanil is noted to be 2–5 min [37]. Doses of fentanyl would typically be 2–4 µg/kg. Lidocaine 0.5–1 mg/kg can also be used for reducing this sympathetic response.

An understanding of the physiology of one-lung ventilation (OLV), the strategies for inducing OLV, and the means to address intraoperative challenges associated with OLV is required to improve operative efficiencies and patient outcomes.

A plan to maintain a patent airway and adequate ventilation at all times will ensure maintenance of hyperoxia and normocarbia. To this effect, mask ventilation needs to be rapidly established after loss of consciousness; and neuromuscular blockade rapidly induced – to accommodate the reduction in functional residual capacity (FRC), which shortens the apneic oxygenation time in these patients. Sevoflurane is initially employed in patients with reactive airways disease until sufficient depth of anesthesia is obtained. No significant outcome differences have been established in terms of maintenance of anesthesia for currently used volatile agents, such as isoflurane, sevoflurane, and desflurane (see HPV).

If the patient is scheduled for a diagnostic bronchoscopy, a laryngeal mask airway (LMA) may be placed. This allows the upper airway to also be assessed for associated smoking-related laryngeal cancers. However, if the patient is scheduled for a mediastinoscopy, a standard single lumen endotracheal tube (preferably 8.0 mm, internal diameter) may be preferred. Once bronchoscopy and/or mediastinoscopy are complete, lung isolation using a DLT or bronchial blocker needs to be implemented to facilitate the thoracotomy. The endotracheal tube (DLT or single lumen tube with bronchial blocker) should then be secured with tape to the nondependent side, allowing easy access to the tape if the tube needs to be repositioned while in the lateral decubitus position. The patient is then positioned in the lateral decubitus position, 100% FiO₂ maintained, and lung isolation then established. Proper positioning of the endotracheal tube should be reconfirmed after the patient's repositioning, because flexion or extension of the neck can potentially displace the endotracheal tube. The "tip of the tube follows the tip of the nose"; therefore, head extension causes the endotracheal tube to move proximally, and the endobronchial balloon can herniate across the main carina. Confirmation of tube position with fiberoptic bronchoscopy after placement and position change decreases the incidence of inadequate lung isolation.

The use of a left double lumen endotracheal tube for a left thoracotomy carries the increased risk of acute intraoperative hypoventilation if the endotracheal tube displaces proximally with the endobronchial balloon herniating across the carina. This can also occur from overinflation of the endobronchial balloon. The astute anesthesiologist may notice decreased tidal volumes as the balloon partially obstructs the right main stem orifice. Minute ventilation alarms may be triggered if there is a partial occlusion, or the high-pressure alarms will be triggered if there is a total or near total occlusion. The anesthesiologist reacts based on the patient's oxygenation and the surgeon's flexibility. If the patient is appropriately oxygenated, then ventilation can be briefly suspended and the fiberoptic bronchoscope utilized to check tube position and the endobronchial cuff deflated prior to tube advancement. If the patient deoxygenates acutely to dangerously low levels, then quick communication should inform the surgeon of the urgent need to re-establish two-lung ventilation. This is achieved by re-establishing ventilation through both the tracheal and endobronchial lumens of the DLT and, importantly, by deflation of

the endobronchial balloon. The endotracheal tube can then be repositioned and OLV re-established once oxygenation levels are satisfactory.

OLV strategies are covered in detail in Chaps. 6 and 21. Briefly, the patient is maintained on 100% oxygen (or combined with nitrous oxide) during initial two-lung ventilation. This denitrogenation allows for faster deflation – through absorption atelectasis – of the nondependent (surgical) lung on the initiation of OLV. ALI increases with greater peak inspiratory pressures [38, 39]. Ventilation parameters during OLV therefore typically strive to reduce the risk of ALI associated with barotrauma or volutrauma through tidal volume reduction (<6 mL/kg), respiratory rate >10 breaths per minute, I:E ratio of 1:2, and peak inspiratory pressure <25 mmHg. Such a protective ventilatory strategy aims to maintain baseline CO_2 levels or tolerate permissive hypercapnia ($\text{pH} > 7.25$) rather than mild hypocapnia. This protective ventilatory strategy is supported by evidence that reduced tidal volume (5 mL/kg) during OLV decreases the proinflammatory systemic response, improves lung function, and results in earlier extubation after esophagectomy [40]. Similarly, mechanical ventilation with lower tidal volumes (6 mL/kg and 10 cm H_2O positive end expiratory pressure; PEEP) after 5 h of two-lung mechanical ventilation is noted to induce lowered activation of bronchoalveolar coagulation, as reflected by reduced thrombin–antithrombin complexes, soluble tissue factor, and factor VIIa levels in lavage fluids when compared to higher tidal volumes (12 mL/kg ideal body weight) without PEEP [41, 42].

In patients with significant COPD with a prolonged exhalation phase and CO_2 retention, the respiratory rate and I:E ratio need to be adjusted to avoid hyperexpansion from breath stacking. In patients with right ventricular dysfunction or pulmonary hypertension, ventilator parameters should aim to maintain hyperoxia and induce mild hypoxemia in an attempt to reduce pulmonary vasoconstriction and any further strain on the right heart.

Optimal ventilation can be achieved by maintaining an appropriate plane of anesthesia to decrease the risk of reactive airways, inducing neuromuscular blockade to prevent abdominal or chest wall contractions, suctioning the double lumen to prevent mucus plugs, and visual bronchoscopic checks of the tube placement to correct tube malposition, kinking, and misalignment.

Typically, for a patient on 100% oxygen, the initiation of OLV does not bring on any immediate changes except for changes in ventilatory pressures or parameters. Oxygenation is maintained due to apneic oxygenation. The duration of apneic oxygenation is proportional to the FRC and dependent on oxygen utilization. This can last a few minutes in COPD patients with reduced FRC or longer (8–15 min) in healthy nonsmokers. Once the nondependent lung is bereft of oxygen, a shunt develops and hypoxemia can ensue. HPV (discussed below) is initiated by the mitochondria sensing decreased oxygen levels.

Should hypoxia develop during OLV, the first response should be to communicate the same to the surgeon in case two-lung ventilation needs to be resumed. Delivery of 100% oxygen through a properly positioned endotracheal tube needs to be ensured. Assuming that the rate of descent of the saturation is not too rapid and the nadir is safe (moderate hypoxemia, 88–90% saturation), then the nadir can be tolerated for several minutes until HPV has a chance to decrease the shunt. If unsafe levels of hypoxemia are reached, then the shunt needs to be decreased. This can be achieved through the application of CPAP, with 100% O_2 delivery to the nondependent lung. PEEP to the dependent lung can eliminate atelectasis, but this typically has a lesser impact on saturation than does CPAP. Restoration of adequate cardiac output and blood pressure can also restore oxygenation by improving the blood flow (perfusion zones) and V/Q matching in the dependent lung. It is important to advise the surgeon to any changes in ventilation, particularly when they are dissecting around the hilum. Obviously, if the oxygen saturation falls to a dangerous level then either two-lung ventilation needs to be resumed or a temporary clamp on the pulmonary artery of the nondependent lung can be placed. While the temporary pulmonary artery clamp will significantly reduce the shunt, extreme care should be taken as it can incite right heart strain and right heart failure.

After positioning the patient, prior to surgery, the multidisciplinary (anesthesia, surgical, and nursing) team should “time out” and pause for open dialog to ensure that the correct patient, correct surgical side, sterility of instruments, patient safety procedures (including surgical site marking, thromboembolic prophylaxis, strategies to maintain normothermia, antibiotic administration within 1 h prior to incision, type and screen for blood cross-matching, correct surgical instruments, etc.) are verified and to provide an opportunity to address any potential concerns that need clarification or may harm the patient. In the future, computerized information technology (anesthesia information management systems, AIMS) will increasingly assist supportive decision making, with smart alerts prompting for critical items such as timely antibiotic administration, risk prediction modeling, and allow benchmarking against national outcomes databases.

At rest, the normal pulmonary vascular system is noted as a high-compliance, high-flow, low-pressure system. This contrasts the systemic circulation, which has much higher resting levels of arterial and venous tone. This difference stems partly from the anatomy because the pulmonary precapillary arterioles have a thinner media and less smooth muscle than their systemic counterparts. Furthermore, at rest, there are far more recruitable vessels in the pulmonary bed that allow dramatic increases in flow with minimal impact on pressure.

The difference between the systemic and arterial systems is also due to the way in which the pulmonary vascular endothelium responds to the challenges of hypoxia (HPV). This vasoconstriction is known as the Euler–Ljestrond reflex. While the basic mechanism of HPV is controversial, it appears that mitochondria play a key role as the primary sensors of hypoxia,

with intracellular calcium levels increasing as a key response [43]. Voltage-gated K⁺ channels directly alter mitochondrial responses. L-type Ca²⁺ channels are facilitated by the depolarization of the K⁺ channels, and they directly increase intracellular Ca²⁺. Classical transient receptor potential channel 6 (TRPC6) also increases intracellular Ca²⁺ as do store-operated channels (SOC) and Na⁺/Ca²⁺ exchangers (NCX) [43]. This rise in intracellular Ca²⁺ triggers further Ca²⁺ release from the sarcoplasmic reticulum via activation of the ryanodine receptors. The end result is constriction of the smooth muscle of the precapillary sphincters and pulmonary arterioles. This calcium-dependent vasoconstriction is the primary phase of HPV and lasts 15–30 min. The calcium-independent phase (the sustained phase) of pulmonary vascular constriction starts at 15 min and can last for several hours. It is highly dependent on RhoA/Rho kinase (ROCK)-mediated Ca²⁺ sensitization [44], and may play a key role in the development of pulmonary hypertension [45]. Interestingly, NO-induced relaxation and endothelin-1-induced vasoconstriction of pulmonary arteries has been demonstrated to be due to the regulation of ROCK-mediated Ca²⁺-sensitization, rather than altered Ca²⁺ metabolism [46, 47].

End tidal CO₂ can influence HPV. Alveolar hypercapnea, but not arterial hypercapnea, can inhibit NO synthetase [48]. This inhibition augments the increase in pulmonary vascular tone following endothelin-induced vasoconstriction. Consequently, mild hypercapnea can reduce shunt. However, hypoventilation can worsen hypoxemia, as can right heart strain and decreasing cardiac output.

Anesthetics can influence pulmonary vascular function and inhibit HPV. Inhalational agents (halothane and enflurane; and to a lesser degree, isoflurane, desflurane, and sevoflurane) will inhibit HPV, but at concentrations of greater than 1 MAC [49]. Propofol may have a less profound impact on HPV than the inhalational agents [50], but this effect is not significant when a BIS of 40–60 is targeted [51]. Opioids, benzodiazepines, and epidural and paravertebral analgesics/anesthetics have minimal impact. Normothermia, mild hypercapnia, and mild acidosis may enhance HPV. Direct vasodilators such as sodium nitroprusside and nitroglycerine should be avoided as they abolish HPV, thus increasing the shunt and causing hypoxemia [44, 49]. Antihypertensives such as beta-blockers, calcium channel blockers, and angiotensin-converting enzyme (ACE) inhibitors may theoretically reduce HPV but have minimal impact in clinical practice [44, 49].

It is unlikely that the routine patient would tolerate the sole use of regional anesthesia, especially during an open thoracotomy. The techniques of general and epidural or paravertebral anesthesia often are combined to utilize the benefits of each. The relative contribution of each technique to combined anesthesia can vary. The regional block may either be used for postoperative analgesia or as the major anesthetic, with light general anesthesia used for amnesia and sedation. Regional block has the advantages of reduction in afterload, improved pulmonary function [52–56], decreased incidence of venous

thromboembolism [52, 57, 58], and suppression of the stress response [56, 59–62]. Potential disadvantages include the time required to establish the block, potential increased fluid requirements, relative decrease in blood pressure associated with sympathectomy, and the potential for adverse complications such as epidural hematoma.

A prospective, randomized, controlled clinical study has previously examined the effects of epidural anesthesia and postoperative analgesia on the postoperative morbidity rate in high-risk surgical patients [63]. Patients who received epidural anesthesia and analgesia had fewer overall complications and fewer cardiovascular or major infectious complications, lower urinary cortisol secretion (a marker of the stress response), and lower hospital costs [63]. Vital capacity and lung compliance are known to decrease after general anesthesia and neuromuscular blockade in patients undergoing thoracotomy. Epidural analgesia with light general anesthesia results in a comparatively lesser decrease in static compliance and fewer alterations in postoperative pulmonary function [64, 65]. The perioperative use of epidural anesthesia is also associated with fewer major postoperative infections. This may result from (1) the decreased duration of endotracheal intubation and mechanical ventilation, which diminishes many of the defense mechanisms against infection [66, 67]; (2) decreased duration of intensive care unit (ICU) stay postoperatively and reduced risks of nosocomial infection; and (3) suppression of the endocrine stress response to the surgery, which has an inhibitory effect on the immune system. Immune competence is better preserved postoperatively when epidural anesthesia is used compared with other anesthetic/analgesic techniques [59, 61, 62]. Epidural anesthesia is also reported to be associated with fewer cardiovascular complications, such as a lower incidence of congestive heart failure [64] and decreased size of myocardial infarctions, which are probably related to improved regional subendocardial perfusion [60, 68, 69]. Possible mechanisms for the improved function include afferent sensory blockade, decreased adrenergic tone, and coronary and systemic vasodilation with a reduction in cardiac preload and afterload [60, 68, 69].

The timing of initiation of regional anesthetic is a mildly contentious issue. There has been no consistent benefit from a preemptive analgesic approach when measuring long-term outcomes (chronic pain, survival, readmission, etc.) where the regional anesthetic is established well prior to surgical incision [18, 70–73]. Similarly, it remains unclear what the concentration of intraoperative local anesthetics should be, since concentrations of bupivacaine an order of magnitude apart (0.5–0.05%) have similar short- and long-term pain outcomes as well as similar morbidity and mortality [70–73]. It is considered that if an epidural is employed, a thoracic epidural and a combination of local anesthetics and opioids [74] are superior to local anesthetics or opioids alone. For paravertebral blockade there is no advantage of adding opioids to local anesthetics [75]. A real advantage of utilizing a combined regional and general anesthetic approach is the ability to

limit the amount of inhaled anesthetics, thereby theoretically reducing the inhibition of HPV. The risk of hypotension is reduced with a paravertebral catheter as compared to an epidural catheter [34], but even with an epidural it can be easily managed with alpha agonists and minimal fluid therapy.

Maintenance of anesthesia during thoracic surgery requires attention to the activities of the surgeon. Given the typically long time between induction and incision, epidural or paravertebral bupivacaine loaded after incision should blunt the majority of sympathetic stimulation from the incision and retractor insertion. Manipulation of visceral pleura and the bronchi, which have vagal and phrenic afferents, is not blocked by the epidural; accordingly, these may require supplemental inhalational or intravenous agents.

Volatile, halogenated anesthetic drugs have several desirable properties for use during thoracic procedures. They decrease airway irritability and obtund airway reflexes in patients who usually have reactive airways, and they maintain adequate anesthesia while allowing increased inspired oxygen concentrations. They can be eliminated rapidly, allowing tracheal extubation in the operating room with less concern for postoperative respiratory depression. Although volatile anesthetics allow high inspired O_2 concentrations, they may reduce PaO_2 by increasing the shunt caused by the partial inhibition of HPV. Because large intrapulmonary shunts are anticipated with the initiation of OLV, it is prudent to increase the inspired concentration of oxygen. Nitrous oxide should be avoided in patients who have marginal preoperative oxygenation or in those with large bullae and emphysematous lungs to avoid expansion of bullae by nitrous oxide.

The management of perioperative fluid therapy remains controversial without conclusive data to guide treatment [76]. The origins of the controversy stem from the significant risk of mortality in patients who develop ALI (previously also termed “postpneumonectomy pulmonary edema”) after thoracic surgery. Retrospective reviews have highlighted the possible role of fluid management in the development of ALI, with large volumes of crystalloid and blood component therapy predicting postpneumonectomy pulmonary edema in regression analysis [77]. Obviously, these predictors can simply represent more complex surgery on sicker patients. However, typical guidelines that are promulgated suggest minimizing crystalloid therapy by not replacing the overnight losses, utilizing alpha agonists rather than fluid boluses to compensate for vasodilatation from regional anesthesia, disregarding low urine output, and consider utilizing appropriate blood transfusion to replace lost blood [38, 78]. These guidelines appear prudent, especially given that concomitant smoking-related cardiac disease can decrease systolic function, and potentiate right heart strain from surgery and associated changes in pulmonary vascular resistance.

In brief, much data has been accumulated to suggest that perioperative ALI is an inflammatory response to perioperative stress [39, 79]. Regardless of the volume of fluid, 0.9% (normal) saline appears to induce a stress response in research

settings [80]. However, since there is little data to suggest that other balanced salt solutions would result in an improved outcome, the use of colloids to reduce overall extracellular fluid gain seems reasonable. The concern over the antiplatelet/antithrombotic effect of hydroxylethyl starch results from the effects of the early high-molecular weight compounds, the so-called HES 200/0.5 when dosed greater than 15 mL/kg [81–83]. The newer formulation with small starch particles, the HES 130/0.42, has fewer risks and may be a better alternative to older HES formulations and large-volume crystalloid therapy for blood loss that needs replacement. Albumin therapy probably has an insignificant role in perioperative fluid management unless a large volume of pleural effusion or peritoneal effusion has been drained at the time of surgery [84, 85].

Overall, perioperative fluid management goals for a lobectomy or pneumonectomy attempt to maintain a euvolemic state – favoring fluid restriction (~1.0–1.5 L total crystalloid) and the judicious use of vasoconstrictors such as phenylephrine to provide hemodynamic stability, in an attempt to preserve renal function. Although large volumes of blood loss are rare, any blood loss should be replaced with packed red blood cells. Fresh frozen plasma should only be considered when directed by perioperative testing indicating coagulopathy. Platelet therapy is rarely indicated except in the case of severe thrombocytopenia or perioperative platelet inhibitors associated with widespread oozing, where there are few other therapeutic choices available.

Postoperative Care

On the basis of the evidence available showing improved postoperative outcomes with aggressive postoperative management in high-risk general surgical patients [86] and thoracic surgery patients [87], a decision-making algorithm may guide the need for elective admission into a high dependency unit (HDU) or ICU postoperatively [87]. Proposed criteria include the following: age >70 years; those at increased risk of general anesthesia, as judged by ASA risk score, performance status scores, and cardiovascular risk assessment; and those patients with preexisting fibrotic lung disease. Patients undergoing OLV, especially with a predicted postoperative forced expiratory volume in one second (FEV_1) of less than 44%, and those undergoing extensive lymphatic dissection, should be monitored closely for signs of ALI in the first 5 days postoperatively. These high-risk categories, together with any indication of postoperative complications such as bronchopleural fistula (BPF) or empyema, should mandate immediate transfer to the ICU.

Early identification of high-risk individuals will allow close monitoring and early institution of therapy during the “golden hours” immediately following surgery. Such therapy may include early goal-directed therapy with hemodynamic optimization, early institution of CPAP for hypoxemia, aggressive pain management, and early mobilization. Such strategies

are expected to improve postoperative outcomes and shorten length of hospital stays.

Lung Cancer

Lung cancer is currently the most common cause of cancer mortality throughout the world, with 219,440 new cases diagnosed and 159,390 deaths reported in the U.S. in 2009. The World Health Organization (WHO) classification of lung tumors, revised most recently in 2004, remains the foundation for lung carcinoma nomenclature [88]. Lung cancer is divided into two broad categories: small cell lung carcinoma (SCLC, ~20%) and nonsmall cell lung carcinoma (NSCLC, ~80%). Less common, are other types of cancers, e.g., bronchial carcinoid tumors (~5%). SCLC has been demonstrated to have a strong correlation with cigarette smoking [89]. NSCLC comprises several broad categories based on histology: adenocarcinoma (25%), squamous cell carcinoma (SCC, ~35%), large cell carcinoma, and adenosquamous carcinoma [89].

Intrathoracic Manifestations

The clinical manifestations of lung cancer are varied. Common symptoms include shortness of breath, hemoptysis, chest pain, and increasing dyspnea. Pleural effusions are a common but nonspecific finding observed on chest radiographs. Such effusions result from obstruction of lymphatic drainage or malignant extension of the tumor to the lung surface. Chest pain associated with lung cancer is generally a dull or mild nonspecific pain occurring ipsilateral to the tumor. Metastasis to the chest wall and ribs can result in local tenderness and pleuritic chest pain. Shoulder pain may result from tumor growth at the lung apex and invasion or encroachment of the brachial plexus (such as in Pancoast's tumor). Tumor extension into the pericardium can result in pericarditis, cardiac arrhythmias, and pericardial effusions that cause tamponade. In addition, superior vena cava obstruction by local growths or lymphatic metastases would impede venous return from the head and upper extremities. Other manifestations of lung cancer include neurologic symptoms caused by mechanical encroachment or invasion of the nerve plexus. Involvement of the brachial plexus may result in not only shoulder pain but also upper arm weakness. Involvement of the phrenic nerve can lead to unilateral diaphragmatic dysfunction, and involvement of the recurrent laryngeal nerve can result in hoarseness.

Extrathoracic Metastatic Manifestations

Common extrathoracic sites of metastases include lymph nodes, brain, bone, liver, skin, and adrenal glands [90]. The neurologic manifestations of metastatic brain tumors include hemiplegia, personality changes, cerebellar disturbances, seizures, headache, and confusion. Metastases to bone occur

primarily in the ribs, vertebra, humerus, and femur. Although metastases to the spinal cord and vertebral column are less common, they have implications for positioning and postoperative management of pain.

Extrathoracic Nonmetastatic Manifestations

The extrapulmonary manifestations of lung cancer affect the metabolic, neuromuscular, skeletal, dermatologic, vascular, and hematologic systems. Although uncommon, the systemic manifestations of such paraneoplastic syndromes, especially the metabolic and neuromuscular manifestations, and other nonspecific findings such as malaise, weight loss, and cachexia, may affect perioperative management and impact the patient's recovery and survival.

Metabolic manifestations result from endocrine secretions by the tumor as follows: [91–94]

- Adrenal corticotrophic hormone (ACTH, Cushing's syndrome): most often associated with small cell carcinoma [95].
- Antidiuretic hormone (syndrome of excessive ADH): associated with small cell carcinoma; it may manifest as nausea, vomiting, anorexia, hyponatremia, seizures, or other neurologic disturbances.
- Serotonin (Carcinoid syndrome): diagnosed by elevated 5-hydroxyindoleacetic acid (5-HIAA).
- Parathyroid hormone-like polypeptide: associated with bronchogenic carcinoma; results in hypercalcemia and hypophosphatemia.
- Ectopic gonadotropin production and hypoglycemia are more rare manifestations.

Neuromuscular manifestations are the most frequent extrathoracic nonmetastatic effects of lung cancer, most often associated with small cell carcinoma of the lung [90, 96]. The paraneoplastic myopathy, Eaton-Lambert syndrome, may appear as a myasthenic-like syndrome characterized by proximal muscle weakness, particularly of the pelvic and thigh muscles. The defect in neuromuscular transmission is a result of an antibody-mediated impairment in presynaptic neurocalcium channel activity, which reduces the release of acetylcholine [96]. Patients with this syndrome do not respond as well to anticholinesterase drugs as do patients with myasthenia gravis. In contrast, these patients exhibit an increased sensitivity to succinylcholine and nondepolarizing muscle relaxants.

Other neuromuscular manifestations include subacute cerebral degeneration, encephalomyopathy, and polymyositis. The cause and the pathogenesis of these neuropathies are not completely understood. Immunologic factors are believed to be important in the pathogenic process, because antibody and T-cell responses are directed against shared antigens that are ectopically expressed by the tumor, but otherwise exclusively expressed by the nervous system [90, 97].

In general, these extrathoracic symptoms resolve and laboratory studies return to normal after successful tumor resection.

Treatment Options

SCLC tumors often have distant metastases at the time of diagnosis and are therefore managed primarily by chemotherapy. Only ~50% of people with SCLC survive for 4 months without chemotherapy. With chemotherapy, their survival time is increased by 4–5-fold. Chemotherapy may be given alone, as an adjuvant to surgical therapy, or in combination with radiotherapy. While a number of chemotherapeutic drugs have been developed, the platinum-based class of drugs has been the most effective in the treatment of lung cancers. Chemotherapy alone is not particularly effective in treating NSCLC, but it may prolong survival when NSCLC has metastasized.

Radiation therapy may be employed as a treatment for both NSCLC and SCLC. Radiation therapy may be given as curative therapy, palliative therapy (using lower doses of radiation than with curative therapy), or as adjuvant therapy in combination with surgery or chemotherapy. Radiation therapy can be administered if a person refuses surgery, if a tumor has spread to areas such as lymph nodes or the trachea – making surgical removal impossible, or if a person has other conditions that disallow major surgery. Radiation therapy generally only shrinks a tumor or limits its growth when given as a sole therapy; however, in 10–15% of patients it leads to long-term remission and palliation of the cancer. Combining radiation therapy with chemotherapy can further prolong survival.

NSCLC tumors are more localized and thus better candidates than other types of tumors for curative resection. Surgical removal of the tumor is generally performed for limited-stage NSCLC (Stage I or some Stage II, see Chap. 2, Table 2.6) [98]. About 10–35% of lung cancers can be removed surgically, but removal does not always result in a cure, since the tumors may already have spread and can recur. Lobectomy, the surgical removal of an anatomic lung segment, is generally accepted as the optimal procedure for early-stage NSCLC because of its ability to preserve pulmonary function [98]. Limited (sublobar, segmentectomy) resection is increasingly used to treat patients who cannot tolerate a full lobectomy because of severely compromised pulmonary function, advanced age, or extensive medical comorbidities. Among people who have an isolated, slow-growing lung cancer resected, the 5-year survival is 25–40%. In addition to surgery, adjuvant chemotherapy may be administered for selected patients with Stage IB and Stage II disease [99, 100]. Current research focuses on biomarkers and genetic markers that would predict the response to therapy and may also point to novel treatments [101, 102].

Anesthesia and Long-Term Cancer Outcomes

It is increasingly recognized that anesthetic factors (volatile agents, opioid analgesics, surgical neuroendocrine response, blood transfusion, etc.) may shift the balance toward the progression of residual disease after potentially curative cancer surgery [103–105]. Anesthetics may inhibit both cellular and humoral immune functions through the impairment of neutrophil, macrophage, T cell, and natural killer cell functions.

Regional analgesia attenuates these adverse events by largely preventing the neuroendocrine surgical stress response and minimizing the amount of volatile anesthetic and opioids required. Preliminary animal and human data suggest that regional analgesia may reduce tumor recurrence after cancer surgery [106].

Other perioperative strategies that may impact long-term cancer outcomes seem to focus on antiinflammatory pathways. Statins, via the inhibition of the rate-limiting step of the mevalonate pathway, have potential anticancer effects [107, 108]. There is some evidence for the anticancer effects of statins in patients with esophageal [109] and lung cancer [110, 111]. Additionally, other agents with known antiinflammatory effects also point to the potential for improved outcomes in cancer patients. In this regard, aspirin use is reported to be associated with prolonged survival in breast cancer patients [112], while the perioperative use of antiinflammatory agents (Cox-II inhibitor use in lung cancer; aprotinin use in mesothelioma) [113, 114] is associated with improved postoperative survival. Moreover, the use of regional analgesia is commonly employed in the thoracic surgery population and has been associated with attenuation of metastasis and improvement in recurrence rates for some types of cancers [115–117]. It is imperative that further research is conducted in this field as we strive to improve long-term outcomes.

Surgical Procedure

To allow anesthesiologists to function within the combined expertise of the multidisciplinary team and to ensure optimal patient safety and outcome, a thorough understanding of the salient features of procedure-specific issues is required.

Pulmonary Resection

In most thoracic surgery practices, approximately two-thirds of surgical interventions are related to the management of intrathoracic malignancy or clinical sequelae of cancer. Anatomic resections (segmentectomy, lobectomy, and pneumonectomy) are most commonly performed for lung cancer, while nonanatomic resections (wedge) are typically performed for pulmonary nodules with diagnostic or therapeutic intention. Lobectomy with mediastinal lymph node dissection remains the standard surgical recommendation for the technical management of lung cancer. Segmental resection is a sound oncological operation that is typically used in patients with smaller cancers and marginal pulmonary reserve, such as those patients with COPD [118]. Pneumonectomy offers some more unique possible challenges including a higher mortality rate. The mortality rate of pneumonectomy is 8–10% vs. 2% for lobectomy [119].

Pulmonary resections can be performed via an open or thoracoscopic approach. The technical aspects of the resection are essentially identical whether by an open or thoracoscopic approach. Evolution of surgical technique and technical advances in electronics and instrumentation has renewed

interest in thoracoscopy, especially video-assisted thoracic surgery (VATS). As such, thoracoscopy permits the visualization of the pulmonary cavity through several small portals. These portals provide access for the video camera and allow manipulation of thoracic structures and use of surgical instruments such as staplers, dissectors, coagulators, and lasers. Although initially used for only minor surgical procedures, the application of VATS has expanded considerably for both diagnostic and therapeutic procedures and increasingly utilized in anatomic (lobectomy, segmentectomy) and limited (wedge) resections in selected patients.

Data suggests that VATS procedures may offer advantages beyond open thoracotomy, including decreased postoperative pain, reduced pulmonary impairment, reduced postoperative morbidity, shortened hospital stay, and potentially improved 1-year survival [120, 121]. If access is inadequate or if bleeding complications occur, a thorascopic approach is easily converted to a limited open thoracotomy. VATS procedures for larger resections such as lobectomy seem to derive benefit from more aggressive pain management strategies and epidural techniques may be beneficial. As such, careful communication between surgeon, patient, anesthesiologist, and the acute pain service is warranted to determine the best pain management strategy for each patient.

A thorough physiological assessment with attention to physiological and cardiac reserve is required prior to proceeding with surgical therapy. Spirometry, quantitative ventilation-perfusion scanning, and exercise cardiopulmonary testing can be helpful to determine physiological reserve for resection considerations. When considering pulmonary resection, a postoperative predicted FEV_1 or D_LCO of greater than 40% is a general requirement for resection considerations. In this regard, patients whose preoperative FEV_1 or D_LCO is less than 60% predicted, a quantitative lung scan is performed to determine the predicted postoperative lung function. If the predicted postoperative FEV_1 or D_LCO is greater than 40%, then surgical resection is feasible. In patients with predicted postoperative FEV_1 or D_LCO less than 40%, additional workup with cardiopulmonary exercise testing is required to delineate patient risk. Adequate aerobic exercise capacity (preoperative VO_2 max >15 mL/kg/min and predicted postoperative VO_2 max >10 mL/kg/min or stair climb >3 flights of stairs [54 steps]) improves patients' safety of operation [118]. In those patients who fail to meet these criteria alternatives to resection should be considered. Relative contraindications for pulmonary resection that point to inadequate pulmonary reserve include chronic oxygen use, severe hypercarbia ($PaCO_2 >55$ mmHg), and moderate pulmonary hypertension (PA pressure greater than one-half systemic pressures).

Anesthetic management for pulmonary resection requires effective isolation of the operative lung, judicious fluid management, and an appropriate ventilation strategy of the dependent lung [122, 123]. Intraoperative bleeding is not a common challenge; however, catastrophic hemorrhage can occur in association with pulmonary arterial injury. This necessitates that patients have preoperative typing and screening for potential transfusion, with good venous access and hemodynamic

monitoring – typically an arterial line and two large peripheral cannulae. More central cancers generally increase the risk for an intraoperative event.

The primary cause of perioperative mortality of lung resection remains ALI which can be secondary to infection, transfusion related, pulmonary embolism, but often there is no specific identifiable etiology. Two factors: intraoperative fluid administration and prolonged elevated airway pressures during OLV have been consistently implicated with perioperative lung injury [122, 123]. Optimal intraoperative management of these factors is thus required.

During the conduct of an anatomic pulmonary resection, three structures (the pulmonary artery, pulmonary vein, and bronchus) are identified and divided at the segmental level (segmentectomy), the bronchial level (lobectomy), or the at the mainstem bronchus (pneumonectomy). Prior to division of any structure, there must be assurance that anesthetic "hardware" (endotracheal tubes, suction catheters, nasogastric tube, pulmonary arterial catheters) are absent from the site of resection. Additionally, during the conduct of a segmental resection or lobectomy, patency of the remaining airway must be confirmed prior to airway division. This requires temporary ventilation of the lung in the surgical field to ensure expansion of nonresected segments or lobes. Intraoperatively, chest drains are placed for perioperative management. During chest closure while the patient is still requiring positive pressure ventilation, these drainage catheters should be placed to suction. Provided that postoperative air leak is minimal, most surgeons manage chest drainage tube without suction (i.e., "water seal") [124].

Regardless of the type of pulmonary resection performed, extubation should be planned following surgery. Adequate postoperative analgesia is required to optimize patient outcome by ensuring the patient can cough and has adequate tidal volumes with breathing. As a result, liberal use of thoracic epidural analgesia is encouraged. Resumption of spontaneous breathing will avoid possible lung barotrauma as well as the risk of bronchial stump disruption and resultant BPF formation. Attention to optimal analgesia, pulmonary toilet, and pleural space management is required to achieve optimal patient outcome. Regional analgesia with epidural catheter provides superior pain control and promotes effective pulmonary toilet. Early mobilization is required with ambulation initiated the first postoperative day. Most patients will have a component of underlying reactive airways disease and regular administration of bronchodilator therapy is typically used. Awake, bedside bronchoscopy is used liberally for secretion management. Noninvasive ventilator support, such as CPAP or BiPAP, can be used, but more often, endotracheal intubation is optimal for postoperative respiratory failure so as to decrease risk of aspiration event and subsequent pneumonia.

Lobectomy

Lobectomy with mediastinal lymph node dissection remains the standard surgical recommendation for the technical management of lung cancer. Lobectomy, commonly performed

via open thoracotomy or VATS, is associated with lower local tumor recurrence compared to lesser resections. An open thoracotomy is usually performed through a postero-lateral thoracotomy incision but antero-lateral and muscle-sparing lateral incisions are used occasionally. In cases where the clinical staging of the lung cancer is advanced, an elective lobectomy may be converted to a bi-lobectomy or pneumonectomy during the operation. Potential intraoperative problems include damage to the airway while using lung isolation devices, potential for bleeding, and hypoxemia during OLV.

After the lobe and blood vessels have been dissected, a test maneuver is performed by the surgeon clamping the surgical bronchus and confirming that the correct lobe is extirpated. The anesthesiologist then unclamps the DLT on the respective side, or in the case of a bronchial blocker, deflates the blocker balloon, and re-expands the lung with manual ventilation. During VATS lobectomy, re-inflating the residual lobe may interfere with the surgical field and so the anesthesiologist may be asked to fiber-optically inspect the bronchial tree to confirm patency of the bronchus of the noninvolved lobe. Once the lobectomy has been performed, the bronchial stump is usually tested with 30 cm H₂O positive pressure in the anesthetic circuit to detect the presence of air leaks. Following an uncomplicated lobectomy the patient is usually extubated in the operating room, provided preoperative respiratory function is adequate. Emergence of the patient in a comfortable manner with good inspiratory effort and ability to cough requires aggressive postoperative analgesia, commonly achieved through the use of either a thoracic epidural or through a paravertebral analgesia technique.

Pancoast tumors are carcinomas of the superior sulcus of the lung and can invade/compress local structures including the lower brachial plexus, subclavian blood vessels, stellate ganglion (resulting in Horner's syndrome), and vertebrae. More complicated resection may entail a two-stage procedure with an initial operation for posterior instrumentation/stabilization of the spine. During lobectomy extensive chest wall resection may be required and massive transfusion is a possibility. Peripheral lines and monitoring should be placed in the contra-lateral arm due to frequent compression of the ipsilateral vessels during surgery.

Sleeve Lobectomy

Bronchogenic carcinoma is the most frequent indication for a sleeve lobectomy, followed by carcinoid tumors, endobronchial metastases, primary airway tumors, bronchial adenomas, and occasionally benign strictures. Sleeve lobectomy involving parenchyma-sparing techniques in patients with limited pulmonary reserve, provides an alternative surgery for patients that cannot tolerate a pneumonectomy. The sleeve technique involves mainstem bronchial resection without parenchymal involvement and possibly resection of pulmonary arteries to avoid pneumonectomy (Fig. 22.3). Sleeve resection, with re-implantation of the remaining lobe, associates with

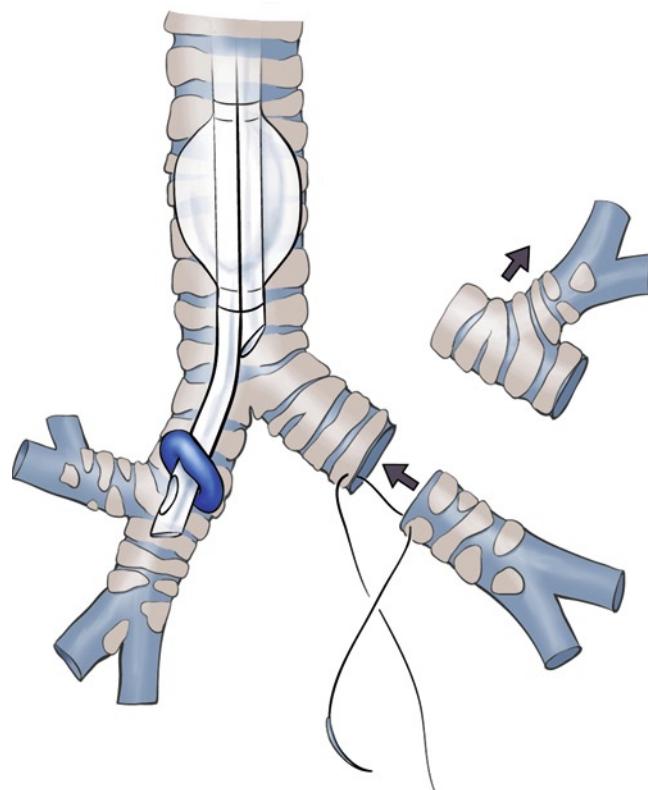


FIG. 22.3. Illustration of a sleeve resection for carcinoma of the left upper lobe, with re-implantation of the left lower lobe.

shorter periods of postoperative mechanical ventilation, shorter duration of ICU stay, fewer loco-regional recurrences, and improved overall survival. Immediate and long-term survival is better after sleeve lobectomy compared with right pneumonectomy for comparable stages of right upper lobe cancer [125].

Ideally, patients undergoing sleeve lobectomy require lung isolation with a contra-lateral DLT or endobronchial tube thereby improving surgical exposure for resection and re-implantation. High-frequency jet ventilation can be used for resections close to the tracheal carina. In rare cases a sleeve lobectomy may require transplant of vessels, thereby necessitating temporary heparinization. In these cases, thoracic epidural catheters should not be manipulated for 24 h following heparin administration. During pulmonary arterioplasty uncontrollable bleeding may occur. For this reason, large bore intravenous catheters should be used. Patients undergoing sleeve lobectomy are usually extubated in the operating room before transfer to the postanesthesia recovery room.

Pneumonectomy

Complete removal of the lung is required when a lobectomy or its modifications (bilobectomy or sleeve lobectomy) is not adequate to remove the local disease and/or ipsilateral lymph node metastases. However, pneumonectomy offers more

unique challenges, including a higher incidence of morbidity (cardiac complications, ALI, ARDS) and mortality (8–10% for pneumonectomy vs. 2% for lobectomy) [119]. The overall operative mortality correlates inversely with the surgical case-volume [126].

The technical conduct of the resection is typical as with any pulmonary resection. The pneumonectomy is usually performed through a standard postero-lateral incision. The mediastinal pleura are incised and the pulmonary artery, the superior and inferior pulmonary veins, and the mainstem bronchus are evaluated for resectability. After all vessels are stapled, stapling of the bronchus occurs and the entire lung is taken from the chest. A test for air leaks is generally performed at this point and reconstruction of the bronchial stump is completed. The bronchial stump should be as short as possible to prevent a pocket for the collection of secretions.

Patients undergoing a pneumonectomy commonly receive a thoracic epidural catheter for postoperative analgesia, unless there is a contraindication. The placement of large bore intravenous lines is necessary in case blood products need to be administered. An invasive arterial line is placed for measurement of beat-to-beat blood pressure and to monitor arterial blood gases. A central venous pressure catheter is recommended to help guide intravascular fluid management, specifically in the postoperative period. Management of lung isolation in a pneumonectomy patient can be achieved with a DLT, bronchial blocker, or single-lumen endobronchial tube. When using a DLT for a pneumonectomy patient, it is preferable to use a device that does not interfere with the ipsilateral airway; however, the preference to use a left-sided DLT (or left-sided bronchial blocker) requires that during a left pneumonectomy these devices are withdrawn prior to stapling the bronchus, in order to avoid accidental inclusion into the suture line.

Challenges can arise related to the empty hemithorax following pneumonectomy. There is no consensus among thoracic surgeons as to the best management of the post-pneumonectomy space. Some thoracic surgeons do not place a chest drain after a pneumonectomy, while others prefer a temporary drainage catheter to add or remove air. The removal of air, ranging from 0.75 to 1.5 L, is necessary to empty the chest and to keep the mediastinum and trachea “balanced” (in the midline). Some surgeons place a specifically designed postpneumonectomy chest drainage system with both high- and low-pressure under-water relief valves to balance the mediastinum. A chest X-ray is mandatory after the patient arrives in the postanesthesia care unit or in the surgical ICU to assess for mediastinal shift. If suction is applied to an empty hemithorax or a chest drain is connected to a standard under-water seal system it may cause mediastinal shift, impingement of venous return to the heart, and hemodynamic collapse. This requires correction with appropriate instillation or evacuation of air from the empty hemithorax. Although rare, cardiac herniation (more common following right pneumonectomy) can occur with catastrophic consequences and need for emergent correction.

The high morbidity and mortality associated with pneumonectomy is predominantly driven by ALI (also previously termed “postpneumonectomy pulmonary edema”), culminating in respiratory failure. While the incidence of ALI after pneumonectomy is only 4%, the mortality rate associated with ALI is 30–50%.

The etiology for ALI seems multifactorial. In a retrospective report by Zeldin et al. [127], the risk factors that were identified for the development of ALI, previously termed “post pneumonectomy pulmonary edema,” were a right-sided pneumonectomy, increased perioperative intravenous fluid administration, and increased urine output in the postoperative period. However, close analysis of Zeldin’s data reveals that only 6 out of 10 cases had full intake and output data. A more recent study by Licker et al. has shown that the excessive administration of intravenous fluids in thoracic surgical patients (more than 3 L in the first 24 h) is an independent risk related to an ALI [128]. Further, the decrease in ventilatory function, increase in pulmonary artery pressure, and pulmonary vascular resistance (right ventricular afterload) may have a significant detrimental effect on right ventricular function [129].

Consequently, in an attempt to reduce high risk for perioperative morbidity and mortality following a pneumonectomy, perioperative management should focus on the judicious management of perioperative fluid therapy, tidal volumes during mechanical ventilation, and improved ICU strategies. In this regard, a recent retrospective review (Table 22.1) suggested that the incidence and mortality of ARDS after lung resection is declining, and likely associated with more aggressive strategies to avoid pneumonectomy, greater attention to protective ventilation strategies during surgery and to improved ICU management of ARDS [2].

A retrospective report [130] involving 170 pneumonectomy patients showed that patients that received median tidal volumes greater than 8 mL/kg had a greater risk of respiratory failure in the postoperative period after pneumonectomy. In contrast, patients that received tidal volumes less than 6 mL/kg were at lower risk of respiratory failure. Schilling et al. [131] have shown that a tidal volume of 5 mL/kg during OLV significantly reduces the inflammatory response to alveolar cytokines. Considering these factors, it is prudent to use lower tidal volumes (i.e., 5–6 mL/kg, ideal body weight) in the pneumonectomy patient and limit peak and plateau inspiratory pressures (i.e., <30 and 25 cm H₂O) during OLV.

The presentation of ALI is biphasic, with intraoperative strategies (fluid restriction and lower tidal volumes) aimed at reducing the incidence of the primary form, which typically has a clinical onset during the first 72 h. The secondary, or late form, appears after 72 h and is usually related to other complications such as aspiration, BPF, or surgical complications. At the present time only symptomatic management is appropriate for ALI, including fluid restrictions, diuretic administration, low ventilatory pressures and tidal volumes (if mechanical ventilation is used), and measures to decrease the pulmonary artery pressure.

Sleeve Pneumonectomy

Tumors involving the most proximal portions of the mainstem bronchus and the carina may require a sleeve pneumonectomy. These are most commonly performed for right-sided tumors and can usually be performed without cardiopulmonary bypass via a right thoracotomy. A long single-lumen endobronchial tube can be advanced across into the left main stem bronchus during the period of tracheo-bronchial anastomosis. High-frequency positive pressure ventilation (has also been used for this procedure). Since the carina is surgically more accessible from the right side, left sleeve pneumonectomies are commonly performed as a two-stage operation, with a left thoracotomy to perform the pneumonectomy and a right thoracotomy to perform the carinal excision. The complication rate and mortality are higher and the 5-year survival significantly lower than for other pulmonary resections. Post-pneumonectomy pulmonary edema is particularly a problem following right sleeve pneumonectomy.

Limited Pulmonary Resections: Segmentectomy and Wedge Resection

Segmentectomy and wedge resection are limited pulmonary resections. Segmentectomy is a sound oncological operation that is typically used in patients with smaller cancers and marginal pulmonary reserve, such as those patients with COPD [118]. It entails an anatomic pulmonary resection of the pulmonary artery, vein, bronchus, and parenchyma of a particular segment of the lung. Lung cancers that are considered for limited resection are usually less than 3 cm in size, located in the periphery of the lung, and with regional lymph nodes free of metastatic cancer.

In contrast, a wedge resection is a nonanatomic removal of a portion of the lung parenchyma with a 1.5–2.0 cm margin, and can be accomplished by open thoracotomy or VATS. Wedge resections are most commonly performed for diagnosis of lung lesions with unknown histology or as palliation in patients with metastatic lesions in the lungs from distant primary tumors.

A group of patients considered for limited pulmonary resection are those who develop a new primary lesion after a previous lobectomy or pneumonectomy. The patient with compromised lung function presents a greater risk in the intraoperative period (hypoxemia during OLV or prolonged intubation after surgery). Cerfolio et al. [132] reported that lung cancer patients with compromised pulmonary function can safely undergo limited pulmonary resection if selected appropriately. Segmentectomies and wedge resections can be performed with any of the standard thoracotomy or VATS incisions. Segments that are most commonly resected are in the upper lobes or the superior segments of the lower lobes.

Anesthetic technique and monitoring are essentially the same as for larger pulmonary resections. In order to facilitate surgical exposure and achieve OLV, it is necessary to

use either a DLT or a bronchial blocker. If the patient had a previous contra-lateral lobectomy or a pneumonectomy selective lobar collapse with the use of a bronchial blocker will facilitate surgical exposure while maintaining oxygenation. In selected cases the combined use of a DLT and a bronchial blocker will allow selective lobar collapse/ventilation in the ipsilateral lung [133]. It is very important to use low tidal volumes (i.e., 3–5 mL/kg) during selective lobar ventilation, particularly in patients with previous pneumonectomy to prevent over-inflation in the remaining lobes.

Segmentectomy plays a significant role in the management of patients with a second primary lung cancer. Many of these patients have previously undergone thoracic surgery, this includes previous lobectomy or pneumonectomy, therefore the potential for increased intraoperative bleeding is always a risk. In addition, because many of these patients have compromised lung function, early extubation may not be feasible. A common complication after surgery is an air leak. Chest tubes are placed to maximize postoperative expansion and minimize space complications. Suction and under-water seal chest drainage is used in the postoperative period.

Bronchopleural Fistula

BPF can result as a consequence of surgical therapy (Fig. 22.4) or from the complications of intrathoracic infection or malignancy (see also Chap. 33). The classic presentation is a patient who has undergone a resection 10–14 days previously, who feels unwell and who has developed a productive cough of “salmon-colored” sputum. Patients can succumb to the resultant soilage of the lung and pneumonitis. If surgical therapy is required for BPF, the surgeon and anesthesiologist must combine their efforts to prevent any further lung injury.

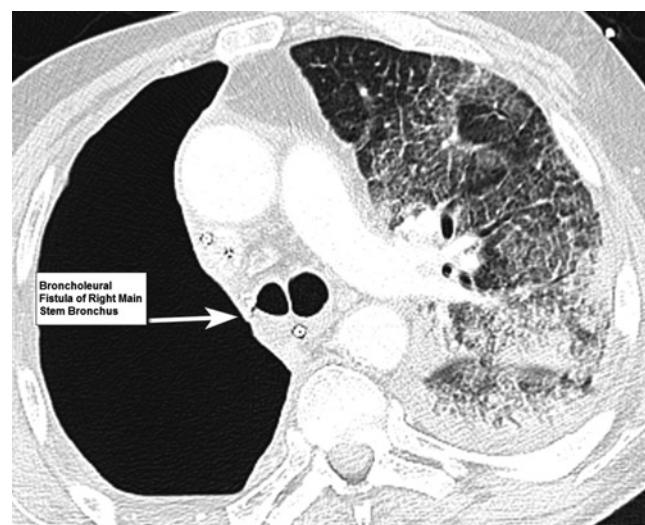


FIG. 22.4. CT image of a bronchopleural fistula in the right main stem bronchus, which developed after pneumonectomy, with accompanying pneumonitis in the contralateral lung.

In order to achieve satisfactory and sustainable ventilation, the team must have a command of the airway options as well as knowledge of nonstandard ventilation strategies. Positive pressure ventilation is achievable in patients with a small fistula. However, with larger fistula, the ability to ventilate without isolating the fistula may be limited, and maintaining spontaneous ventilation may be a requisite. The initial management of the fistula is indeed drainage of the infected pleural space. Patient positioning should be kept in mind, and the side of the fistula should be maintained in a dependent position. Surgical management of the fistula typically involves closure with vascularized flap coverage or window thoracostomy for drainage. Rarely, additional pulmonary parenchyma resection is required. As with tracheal surgical interventions, the use of jet ventilation and appropriate airway isolation strategies could potentially be necessary. Prompt discontinuation of positive pressure ventilation is also required. In fact, if patients need positive pressure ventilation in the presence of a BPF and this provides satisfactory ventilation and oxygenation, the surgical treatment of the BPF is relatively contraindicated.

Clinical Case Discussion

Case: A 68-year-old male presents for anesthesia. He has a 40 pack-year smoking history, hypertension controlled with diltiazem, and hypercholesterolemia controlled with simvastatin. He gives no history of exertional angina. The chest X-ray indicates a mass in the left upper lobe (Fig. 22.5), with absence of metastatic disease as assessed by computerized tomography and by a nuclear bone scan. Pulmonary function testing shows impaired function, characteristic of moderate COPD, with a negligible reversible component and a predicted postoperative FEV₁ of 48%.



FIG. 22.5. Chest X-ray demonstrating a carcinoma of the left upper lobe.

Previous diagnostic bronchoscopy revealed encroachment of a nonsmall cell lung cancer onto the left main stem bronchus. Consequently, he is now scheduled for a bronchoscopy, mediastinoscopy and left upper lobectomy with sleeve resection, and reattachment of the left lower lobe.

Questions:

1. How does the mediastinoscopy alter perioperative management?
2. What airway management technique would be optimal?
3. What invasive monitoring is necessary?
4. Is there an optimal analgesic regimen?
5. Can perioperative fluid management affect outcome?
6. What ventilation strategy would promote optimal outcome?

Discussion:

Given the rarity of blood loss requiring blood transfusion an 18- or 16-gauge intravenous catheter, preferably placed in the nondependent hand, wrist or forearm, would be appropriate. It is best to avoid the antecubital veins as the arms are bent at 90° when the patient is positioned in a lateral decubitus position and this will hamper flow of the intravenous fluids. In anticipation of continuation to thoracotomy after mediastinoscopy a thoracic epidural (alternatively, a paravertebral block) is placed in the T5–T8 region prior to induction. Standard noninvasive monitors will be used, with ECG leads placed as for any median sternotomy, thereby allowing the entire chest to be prepped in a sterile fashion in case an emergent sternotomy is required due to massive bleeding resulting from the mediastinoscopy.

After induction, tailored to the patient, the airway is secured using an 8.0-mm single lumen endotracheal tube to facilitate bronchoscopy. A LMA can be used for bronchoscopy if mediastinoscopy is not required. The endotracheal tube is usually brought out to the side of the mouth closest to the anesthesia machine once the bed is turned 90° for mediastinoscopy.

Given the absence of significant cardiac disease invasive monitoring, with placement of an arterial line, can be deferred until after the mediastinoscopy is completed and the decision is made to proceed to a thoracotomy – based on the absence of mediastinal lymph node involvement by the cancer. Placement of the arterial line is preferred in the dependent radial artery. This allows vigilant hemodynamic monitoring since acute hemodynamic embarrassment often occurs during surgical manipulation and due to the risk of catastrophic pulmonary vasculature injury. Significant fluctuations in blood pressure are especially seen with left-sided procedures where compression of the heart may occur during surgical manipulation.

A right-sided DLT would be of greater advantage in this case. Since a thoracotomy with sleeve resection requires surgical re-implantation of the left lower lobe bronchus (Fig. 22.3), a left-sided DLT may hamper optimal surgical exposure. If intubation is profoundly difficult, to the point where even

changing the endotracheal tube over a tube changer would place the patient at significant risk, then alternative strategies including placement of a left main stem bronchial blocker or advancement of the single lumen endotracheal tube into the right main stem bronchus should be considered.

Clear communication between the surgical and anesthetic team is essential if the pulmonary artery requires resection and reconstruction. In this case blood products should be readily available in the operating room and steps to reduce the pulmonary artery pressure should be implemented. Such steps may include increased oxygenation (FiO_2 , 100%), moderate hypocapnia (PaCO_2 , 30–35 mmHg), an appropriately “deep” level of anesthesia, minimized use of phenylephrine (consider vasopressin if blood pressure is low), and inhaled epoprostenol therapy to the ventilated lung.

Timing of initiation of the epidural and the choice of neuraxial medications remains controversial. A common practice is to initiate the epidural prior to induction so that inhalational anesthetics can be reduced to levels where HPV is not hampered. The intraoperative use of the epidural also helps to minimize the use of systemic opioids to reduce the risk of postoperative respiratory depression. Typically, more concentrated local anesthetics (\pm opioids) are used intraoperatively and more dilute combinations of local anesthetics and opioids used postoperatively.

The management of perioperative fluid therapy remains a controversy without conclusive data to guide treatment. The origins of the controversy stem from the significant risk of mortality from patients who develop ALI after thoracic surgery, in particular, those that develop postpneumonectomy pulmonary edema. Typical guidelines suggest minimizing crystalloid therapy to 1.0–1.5 L, as this may help to reduce postlobectomy pulmonary edema and facilitate early postoperative extubation.

Ventilation parameters during OLV typically strive to reduce the risk of ALI associated with barotrauma or volutrauma through tidal volume reduction (<6 mL/kg), respiratory rate >10 breaths per minute, I:E ratio of 1:2, and peak inspiratory pressure <25 mmHg. Such a protective ventilatory strategy aims to maintain baseline CO_2 levels or tolerate permissive hypercapnia ($\text{pH} > 7.25$) rather than mild hypocapnia. Importantly, prolonged positive pressure ventilation may hamper the tenuous blood supply of the sleeve anastomosis, and increase the risk for a BPF and its associated complications. As such, this necessitates that the overall anesthetic technique be tailored to afford prompt and comfortable extubation of the patient.

References

- Dulu A, Pastores SM, Park B, Riedel E, Rusch V, Halpern NA. Prevalence and mortality of acute lung injury and ARDS after lung resection. *Chest*. 2006;130(1):73–8.
- Tang SS, Redmond K, Griffiths M, Ladas G, Goldstraw P, Dusmet M. The mortality from acute respiratory distress syndrome after pulmonary resection is reducing: a 10-year single institutional experience. *Eur J Cardiothorac Surg*. 2008;34(4):898–902.
- Lighter DE. Advanced performance improvement in healthcare. Sudbury: Jones and Bartlett Publishers; 2010.
- Kohn LT, Corrigan JM, Donaldson MS. To err is human: building a safer health system. Washington, D.C.: National Academies Press; 2000.
- Institute of Medicine Committee on Quality Health Care in America. Crossing the quality chasm: a new health system for the 21st century. Washington, D.C.: National Academies Press; March 2008.
- Vincent C, Moorthy K, Sarker SK, Chang A, Darzi AW. Systems approaches to surgical quality and safety: from concept to measurement. *Ann Surg*. 2004;239(4):475–82.
- Dimick JB, Pronovost PJ, Cowan JA, Lipsett PA. Surgical volume and quality of care for esophageal resection: do high-volume hospitals have fewer complications? *Ann Thorac Surg*. 2003;75(2):337–41.
- Chowdhury MM, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. *Br J Surg*. 2007;94(2):145–61.
- Dimick JB, Cowan Jr JA, Ailawadi G, Wainess RM, Upchurch Jr GR. National variation in operative mortality rates for esophageal resection and the need for quality improvement. *Arch Surg*. 2003;138(12):1305–9.
- Dimick JB, Cowan Jr JA, Upchurch Jr GR, Colletti LM. Hospital volume and surgical outcomes for elderly patients with colorectal cancer in the United States. *J Surg Res*. 2003;114(1):50–6.
- Verhoeven C, van de Weyer R, Schaapveld M, Bastiaannet E, Plukker JTM. Better survival in patients with esophageal cancer after surgical treatment in university hospitals: a plea for performance by surgical oncologists. *Ann Surg Oncol*. 2007; 14(5):1678–87.
- Zehr KJ, Dawson PB, Yang SC, Heitmiller RF. Standardized clinical care pathways for major thoracic cases reduce hospital costs. *Ann Thorac Surg*. 1998;66(3):914–9.
- Wright CD, Wain JC, Grillo HC, Moncure AC, Macaluso SM, Mathisen DJ. Pulmonary lobectomy patient care pathway: a model to control cost and maintain quality. *Ann Thorac Surg*. 1997;64(2):299–302.
- Khuri SF. Quality, advocacy, healthcare policy, and the surgeon. *Ann Thorac Surg*. 2002;74(3):641–9.
- Khuri SF, Daley J, Henderson WG. The comparative assessment and improvement of quality of surgical care in the Department of Veterans Affairs. *Arch Surg*. 2002;137(1):20–7.
- Ries AL, Make BJ, Lee SM, et al. The effects of pulmonary rehabilitation in the national emphysema treatment trial. *Chest*. 2005;128(6):3799–809.
- Ries AL. Pulmonary rehabilitation and COPD. *Semin Respir Crit Care Med*. 2005;26(2):133–41.
- Ochroch EA, Gottschalk A, Augostides J, et al. Long-term pain and activity during recovery from major thoracotomy using thoracic epidural analgesia. *Anesthesiology*. 2002;97(5): 1234–44.
- Devereaux PJ, Yang H, Yusuf S, and the POISE Study Group. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008;371(9627):1839–47.
- Garcia S, Moritz TE, Ward HB, et al. Usefulness of revascularization of patients with multivessel coronary artery disease before elective vascular surgery for abdominal aortic and peripheral occlusive disease. *Am J Cardiol*. 2008;102(7):809–13.

21. Garcia S, McFalls EO. CON: preoperative coronary revascularization in high-risk patients undergoing vascular surgery. *Anesth Analg.* 2008;106(3):764–6.
22. McFalls EO, Ward HB, Moritz TE, et al. Predictors and outcomes of a perioperative myocardial infarction following elective vascular surgery in patients with documented coronary artery disease: results of the CARP trial. *Eur Heart J.* 2008;29(3):394–401.
23. McFalls EO, Ward HB, Moritz TE, et al. Clinical factors associated with long-term mortality following vascular surgery: outcomes from the Coronary Artery Revascularization Prophylaxis (CARP) Trial. *J Vasc Surg.* 2007;46(4):694–700.
24. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery.[see comment]. *N Engl J Med.* 2004;351(27):2795–804.
25. Beattie WS, Wijeyesundara DN, Karkouti K, et al. Acute surgical anemia influences the cardioprotective effects of beta-blockade: a single-center, propensity-matched cohort study. *Anesthesiology.* 2010;112(1):25–33.
26. Hindler K, Shaw AD, Samuels J, Fulton S, Collard CD, Riedel B. Improved postoperative outcomes associated with preoperative statin therapy. *Anesthesiology.* 2006;105(6):1260–72.
27. Schouten O, Boersma E, Hoeks SE, et al. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med.* 2009;361(10):980–9.
28. Amar D, Zhang H, Heerd PM, Park B, Fleisher M, Thaler HT. Statin use is associated with a reduction in atrial fibrillation after noncardiac thoracic surgery independent of C-reactive protein. *Chest.* 2005;128(5):3421–7.
29. Amar D. Beta-adrenergic blocker withdrawal confounds the benefits of epidural analgesia with sympathectomy on supraventricular arrhythmias after cardiac surgery. *Anesth Analg.* 2002;95(4):1119, author reply 1119.
30. Schouten O, Hoeks SE, Welten GM, et al. Effect of statin withdrawal on frequency of cardiac events after vascular surgery. *Am J Cardiol.* 2007;100(2):316–20.
31. Anon. Rebound risk: aspirin and statin withdrawal. *Consum Rep.* 2005;70(8):48.
32. Collet JP, Montalescot G. Optimizing long-term dual aspirin/clopidogrel therapy in acute coronary syndromes: when does the risk outweigh the benefit? *Int J Cardiol.* 2009;133(1):8–17.
33. Daly DJ, Myles PS. Update on the role of paravertebral blocks for thoracic surgery: are they worth it? *Curr Opin Anaesthesiol.* 2009;22(1):38–43.
34. Joshi GP, Bonnet F, Shah R, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. *Anesth Analg.* 2008;107(3):1026–40.
35. Conlon NP, Shaw AD, Grichnik KP. Postthoracotomy paravertebral analgesia: will it replace epidural analgesia? *Anesthesiol Clin.* 2008;26(2):369–80.
36. Samain E, Biard M, Farah E, Holtzer S, Delefosse D, Marty J. Monitoring expired oxygen fraction in preoxygenation of patients with chronic obstructive pulmonary disease. *Ann Fr Anesth Rèanim.* 2002;21(1):14–9.
37. Servin FS, Billard V. Remifentanil and other opioids. *Handb Exp Pharmacol.* 2008;182:283–311.
38. Slinger P. Update on anesthetic management for pneumonectomy. *Curr Opin Anaesthesiol.* 2009;22(1):31–7.
39. Bigatello LM, Allain R, Gaißert HA. Acute lung injury after pulmonary resection. *Minerva Anestesiol.* 2004;70(4):159–66.
40. Michelet P, D'Journo XB, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology.* 2006;105(5):911–9.
41. Choi G, Wolthuis EK, Bresser P, et al. Mechanical ventilation with lower tidal volumes and positive end-expiratory pressure prevents alveolar coagulation in patients without lung injury. *Anesthesiology.* 2006;105(4):689–95.
42. Determann RM, Royakkers A, Wolthuis EK, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. *Crit Care.* 2010;14(1):R1.
43. Ward J, McMurry I. Mechanisms of hypoxic pulmonary vasoconstriction and their roles in pulmonary hypertension: new findings for an old problem. *Curr Opin Pharmacol.* 2009;9:1–10.
44. Aaronson PI, Robertson TP, Knock GA, et al. Hypoxic pulmonary vasoconstriction: mechanisms and controversies. *J Physiol.* 2006;570(Pt 1):53–8.
45. Rhodes CJ, Davidson A, Gibbs JSR, Wharton J, Wilkins MR. Therapeutic targets in pulmonary arterial hypertension. *Pharmacol Ther.* 2009;121(1):69–88.
46. Weigand L, Sylvester JT, Shimoda LA. Mechanisms of endothelin-1-induced contraction in pulmonary arteries from chronically hypoxic rats. *Am J Physiol Lung Cell Mol Physiol.* 2006;290(2):L284–90.
47. Jernigan NL, Walker BR, Resta TC. Chronic hypoxia augments protein kinase G-mediated Ca²⁺ desensitization in pulmonary vascular smooth muscle through inhibition of RhoA/Rho kinase signaling. *Am J Physiol Lung Cell Mol Physiol.* 2004;287(6):L1220–9.
48. Yamamoto Y, Nakano H, Ide H, et al. Role of airway nitric oxide on the regulation of pulmonary circulation by carbon dioxide. *J Appl Physiol.* 2001;91(3):1121–30.
49. Nagendran J, Stewart K, Hoskinson M, Archer SL. An anesthesiologist's guide to hypoxic pulmonary vasoconstriction: implications for managing single-lung anesthesia and atelectasis. *Curr Opin Anaesthesiol.* 2006;19(1):34–43.
50. Abe K, Shimizu T, Takashina M, Shiozaki H, Yoshiya I. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation [see comment]. *Anesth Analg.* 1998;87(5):1164–9.
51. Pruszkowski O, Dalibon N, Moutafis M, et al. Effects of propofol vs sevoflurane on arterial oxygenation during one-lung ventilation. *Br J Anaesth.* 2007;98(4):539–44.
52. Popping DM, Elia N, Marret E, Remy C, Tramer MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. *Arch Surg.* 2008;143(10):990–9. discussion 1000.
53. Groeben H. Epidural anesthesia and pulmonary function. *J Anesth.* 2006;20(4):290–9.
54. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice [see comment]. *Ann Surg.* 2003;238(5):663–73.
55. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg.* 2002;183(6):630–41.
56. Grass JA. The role of epidural anesthesia and analgesia in postoperative outcome. *Anesthesiol Clin N Am.* 2000;18(2):407–28.
57. De Cosmo G, Aceto P, Gualtieri E, Congedo E. Analgesia in thoracic surgery: review. *Minerva Anestesiol.* 2009;75(6):393–400.
58. Guay J. The benefits of adding epidural analgesia to general anesthesia: a metaanalysis. *J Anesth.* 2006;20(4):335–40.

59. Holte K, Kehlet H. Effect of postoperative epidural analgesia on surgical outcome. *Minerva Anestesiol*. 2002;68(4):157–61.
60. Lewis KS, Whipple JK, Michael KA, Quebbeman EJ. Effect of analgesic treatment on the physiological consequences of acute pain. *Am J Hosp Pharm*. 1994;51(12):1539–54.
61. Kehlet H. The stress response to surgery: release mechanisms and the modifying effect of pain relief. *Acta Chir Scand Suppl*. 1989;550:22–8.
62. Hahnkamp K, Herroeder S, Hollmann MW. Regional anaesthesia, local anaesthetics and the surgical stress response. *Best Pract Res Clin Anaesthesiol*. 2004;18(3):509–27.
63. Yeager MP, Glass DD, Neff RK, Brinck-Johnsen T. Epidural anesthesia and analgesia in high-risk surgical patients. *Anesthesiology*. 1987;66(6):729–36.
64. Clemente A, Carli F. The physiological effects of thoracic epidural anesthesia and analgesia on the cardiovascular, respiratory and gastrointestinal systems. *Minerva Anestesiol*. 2008;74(10):549–63.
65. Bromage P. Spirometry in assessment of analgesia after abdominal surgery. *Br Med J*. 1955;2:589–93.
66. Spray SB, Zuidema GD, Cameron JL. Aspiration pneumonia; incidence of aspiration with endotracheal tubes. *Am J Surg*. 1976;131(6):701–3.
67. Sackner MA, Hirsch J, Epstein S. Effect of cuffed endotracheal tubes on tracheal mucous velocity. *Chest*. 1975;68(6):774–7.
68. Chaney MA. Intrathcal and epidural anesthesia and analgesia for cardiac surgery [see comment]. *Anesth Analg*. 2006;102(1):45–64.
69. Riedel BJ, Wright IG. Epidural anesthesia in coronary artery bypass grafting surgery. *Curr Opin Cardiol*. 1997;12(6):515–21.
70. Gripe S, Tramer MR. Do we need preemptive analgesia for the treatment of postoperative pain? *Best Pract Res Clin Anaesthesiol*. 2007;21(1):51–63.
71. Pogatzki-Zahn EM, Zahn PK. From preemptive to preventive analgesia. *Curr Opin Anaesthesiol*. 2006;19(5):551–5.
72. Gottschalk A, Cohen SP, Yang S, Ochroch EA. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104(3):594–600.
73. Ochroch EA, Gottschalk A. Impact of acute pain and its management for thoracic surgical patients. *Thorac Surg Clin*. 2005;15(1):105–21.
74. George MJ. The site of action of epidurally administered opioids and its relevance to postoperative pain management. *Anesthesia*. 2006;61(7):659–64.
75. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy—a systematic review and meta-analysis of randomized trials.[erratum appears in *Br J Anaesth*. 2007 Nov;99(5):768]. *Br J Anaesth*. 2006;96(4):418–26.
76. Chong PC, Greco EF, Stothart D, et al. Substantial variation of both opinions and practice regarding perioperative fluid resuscitation. *Can J Surg*. 2009;52(3):207–14.
77. Turnage WS, Lunn JJ. Postpneumonectomy pulmonary edema. A retrospective analysis of associated variables [see comment]. *Chest*. 1993;103(6):1646–50.
78. Jackson TA, Mehran RJ, Thakar D, Riedel B, Nunnally ME, Slinger P. Case 5–2007 postoperative complications after pneumonectomy: clinical conference. *J Cardiothorac Vasc Anesth*. 2007;21(5):743–51.
79. Jordan S, Mitchell JA, Quinlan GJ, Goldstraw P, Evans TW. The pathogenesis of lung injury following pulmonary resection.[see comment]. *Eur Respir J*. 2000;15(4):790–9.
80. Polubinska A, Breborowicz A, Staniszewski R, Oreopoulos DG. Normal saline induces oxidative stress in peritoneal mesothelial cells. *J Pediatr Surg*. 2008;43(10):1821–6.
81. Westphal M, James MFM, Kozek-Langenecker S, Stocker R, Guidet B, Van Aken H. Hydroxyethyl starches: different products—different effects. *Anesthesiology*. 2009;111(1):187–202.
82. Boldt J. Modern rapidly degradable hydroxyethyl starches: current concepts. *Anesth Analg*. 2009;108(5):1574–82.
83. Boldt J. Saline versus balanced hydroxyethyl starch: does it matter? *Curr Opin Anaesthesiol*. 2008;21(5):679–83.
84. Ueda H, Iwasaki A, Kusano T, Shirakusa T. Thoracotomy in patients with liver cirrhosis. *Scand J Thorac Cardiovasc Surg*. 1994;28(1):37–41.
85. Ceyhan B, Celikel T. Serum-effusion albumin gradient in separation of transudative and exudative pleural effusions [comment]. *Chest*. 1994;105(3):974–5.
86. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. *Chest*. 1999;116(2):355–62.
87. Jordan S, Evans TW. Predicting the need for intensive care following lung resection. *Thorac Surg Clin*. 2008;18(1):61–9.
88. Beasley MB, Brambilla E, Travis WD. The 2004 World Health Organization classification of lung tumors. *Semin Roentgenol*. 2005;40(2):90–7.
89. Maggiore C, Mule A, Fadda G, et al. Histological classification of lung cancer. *Rays Oct Dec*. 2004;29(4):353–5.
90. Beckles MA, Spiro SG, Colice GL, Rudd RM. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. *Chest*. 2003;123 (1 Suppl):97S–104.
91. Radulescu D, Pripon S, Bunea D, Ciuleanu TE, Radulescu LI. Endocrine paraneoplastic syndromes in small cell lung carcinoma. Two case reports. *J BUON*. 2007;12(3):411–4.
92. Gandhi L, Johnson BE. Paraneoplastic syndromes associated with small cell lung cancer. *J Natl Compr Cancer Netw*. 2006;4(6):631–8.
93. Gerber RB, Mazzone P, Arroliga AC. Paraneoplastic syndromes associated with bronchogenic carcinoma. *Clin Chest Med*. 2002;23(1):257–64.
94. Posner JB, Dalmau J. Paraneoplastic syndromes. *Curr Opin Immunol*. 1997;9(5):723–9.
95. Amer KM, Ibrahim NB, Forrester-Wood CP, Saad RA, Scanlon M. Lung carcinoid related Cushing's syndrome: report of three cases and review of the literature. *Postgrad Med J*. 2001; 77(909):464–7.
96. Pourmand R. Lambert-eaton myasthenic syndrome. *Front Neurol Neurosci*. 2009;26:120–5.
97. Darnell RB, Posner JB. Paraneoplastic syndromes affecting the nervous system. *Semin Oncol*. 2006;33(3):270–98.
98. Endo C, Sagawa M, Sakurada A, Sato M, Kondo T, Fujimura S. Surgical treatment of stage I non-small cell lung carcinoma. *Ann Thorac Cardiovasc Surg*. 2003;9(5):283–9.
99. Fenwick JD, Nahum AE, Malik ZI, et al. Escalation and intensification of radiotherapy for stage III non-small cell lung cancer: opportunities for treatment improvement. *Clin Oncol*. 2009;21(4):343–60.
100. Ikeda N, Nagase S, Ohira T. Individualized adjuvant chemotherapy for surgically resected lung cancer and the roles of biomarkers. *Ann Thorac Cardiovasc Surg*. 2009;15(3):144–9.

101. Custodio AB, Gonzalez-Larriba JL, Bobokova J, et al. Prognostic and predictive markers of benefit from adjuvant chemotherapy in early-stage non-small cell lung cancer. *J Thorac Oncol.* 2009;4(7):891–910.
102. John T, Liu G, Tsao MS. Overview of molecular testing in non-small-cell lung cancer: mutational analysis, gene copy number, protein expression and other biomarkers of EGFR for the prediction of response to tyrosine kinase inhibitors. *Oncogene.* 2009;28 Suppl 1:S14–23.
103. Goldfarb Y, Ben-Eliyahu S. Surgery as a risk factor for breast cancer recurrence and metastasis: mediating mechanisms and clinical prophylactic approaches. *Breast Dis.* 2006;26:99–114.
104. Ben-Eliyahu S, Page GG, Schleifer SJ. Stress, NK cells, and cancer: Still a promissory note. *Brain Behav Immun.* 2007;21(7):881–7.
105. Atzil S, Arad M, Glasner A, et al. Blood transfusion promotes cancer progression: a critical role for aged erythrocytes. *Anesthesiology.* 2008;109(6):989–97.
106. Sessler DI, Ben-Eliyahu S, Mascha EJ, Parat MO, Buggy DJ. Can regional analgesia reduce the risk of recurrence after breast cancer? Methodology of a multicenter randomized trial. *Contemp Clin Trials.* 2008;29(4):517–26.
107. Chan KK, Oza AM, Siu LL. The statins as anticancer agents. *Clin Cancer Res.* 2003;9(1):10–9.
108. Demierre MF, Higgins PD, Gruber SB, Hawk E, Lippman SM. Statins and cancer prevention. *Nat Rev Cancer.* 2005;5(12):930–42.
109. Ogunwobi OO, Beales IL. Statins inhibit proliferation and induce apoptosis in Barrett's esophageal adenocarcinoma cells. *Am J Gastroenterol.* 2008;103(4):825–37.
110. Maksimova E, Yie TA, Rom WN. In vitro mechanisms of lovastatin on lung cancer cell lines as a potential chemopreventive agent. *Lung.* 2008;186(1):45–54.
111. Khurana V, Bejjanki HR, Caldito G, Owens MW. Statins reduce the risk of lung cancer in humans: a large case-control study of US veterans. *Chest.* 2007;131(5):1282–8.
112. Holmes MD, Chen WY, Li L, Hertzmark E, Spiegelman D, Hankinson SE. Aspirin intake and survival after breast cancer. *J Clin Oncol.* 2010;28:1467–72.
113. Norman PH, Thall PF, Purugganan RV, et al. A possible association between aprotinin and improved survival after radical surgery for mesothelioma. *Cancer.* 2009;115(4):833–41.
114. Norman P. Rofecoxib provides significant improvement in survival following lung resection for cancer. *Anesthesiology.* 2008;109:A1586.
115. Exadaktylos AK, Buggy DJ, Moriarty DC, Mascha E, Sessler DI. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology.* 2006;105(4):660–4.
116. Wada H, Seki S, Takahashi T, et al. Combined spinal and general anesthesia attenuates liver metastasis by preserving TH1/TH2 cytokine balance. *Anesthesiology.* 2007;106(3):499–506.
117. Biki B, Mascha E, Moriarty DC, Fitzpatrick JM, Sessler DI, Buggy DJ. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: a retrospective analysis. *Anesthesiology.* 2008;109(2):180–7.
118. American Thoracic Society Guidelines for patient undergoing possible pulmonary resection www.thoracic.org/sections/copd-for-health-professionals/management-of-stable-copd/surgery-in-and-for-copd/surgery-in-the-copd-patient.html. Accessed May 2010.
119. Allen MS, Darling GE, Pechet TT, et al. Morbidity and mortality of major pulmonary resections in patients with early-stage lung cancer: initial results of the randomized, prospective ACOSOG Z0030 trial. *Ann Thorac Surg.* 2006;81(3):1013–9. discussion 1019–1020.
120. Whitson BA, Groth SS, Duval SJ, Swanson SJ, Maddaus MA. Surgery for early-stage non-small cell lung cancer: a systematic review of the video-assisted thoracoscopic surgery versus thoracotomy approaches to lobectomy. *Ann Thorac Surg.* 2008;86(6):2008–16. discussion 2016–2008.
121. Mahtabifard A, DeArmond DT, Fuller CB, McKenna Jr RJ. Video-assisted thoracoscopic surgery lobectomy for stage I lung cancer. *Thorac Surg Clin.* 2007;17(2):223–31.
122. Lytle FT, Brown DR. Appropriate ventilatory settings for thoracic surgery: intraoperative and postoperative. *Semin Cardiothorac Vasc Anesth.* 2008;12(2):97–108.
123. Licker M, Fauconnet P, Villiger Y, Tschopp JM. Acute lung injury and outcomes after thoracic surgery. *Curr Opin Anesthesiol.* 2009;22(1):61–7.
124. Prokakis C, Koletsis EN, Apostolakis E, et al. Routine suction of intercostal drains is not necessary after lobectomy: a prospective randomized trial. *World J Surg.* 2008;32(11):2336–42.
125. Bagan P, Berna P, Pereira JCDN, et al. Sleeve lobectomy versus pneumonectomy: tumor characteristics and comparative analysis of feasibility and results. *Ann Thorac Surg.* 2005;80(6):2046–50.
126. Ramnath N, Demmy TL, Antun A, et al. Pneumonectomy for bronchogenic carcinoma: analysis of factors predicting survival. *Ann Thorac Surg.* 2007;83(5):1831–6.
127. Zeldin RA, Normandin D, Landtwing D, Peters RM. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg.* 1984;87(3):359–65.
128. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97(6):1558–65.
129. Foroulis CN, Kotoulas CS, Kakouros S, et al. Study on the late effect of pneumonectomy on right heart pressures using Doppler echocardiography. *Eur J Cardio Thorac Surgery.* 2004;26(3):508–14.
130. Fernandez-Perez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology.* 2006;105(1):14–8.
131. Schilling T, Kozian A, Huth C, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. *Anesth Analg.* 2005;101(4):957–65.
132. Cerfolio RJ, Allen MS, Trastek VF, Deschamps C, Scanlon PD, Pairolo PC. Lung resection in patients with compromised pulmonary function. *Ann Thorac Surg.* 1996;62(2):348–51.
133. McGlade DP, Slinger PD. The elective combined use of a double lumen tube and endobronchial blocker to provide selective lobar isolation for lung resection following contralateral lobectomy. *Anesthesiology.* 2003;99(4):1021–2.

23

Anesthesia for Video-Assisted Thoracoscopic Surgery

Edmond Cohen

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Key Points

- Limited options to treat hypoxemia during one-lung ventilation (OLV) compared to open thoracotomy. Continuous positive airway pressure (CPAP) interferes with surgical exposure during video-assisted thoracoscopic surgery (VATS).
- Priority on rapid and complete lung collapse.
- Possibility of prolonged periods of OLV. Particularly during the learning phase of the surgical team.
- Decreased postoperative analgesic requirements compared to open thoracotomy.
- Surgical delay in treating major intraoperative hemorrhage.
- The option of doing minor VATS procedures with local or regional anesthesia.

Historical Considerations of Video-Assisted Thoracoscopy

Thoracoscopy involves intentionally creating a pneumothorax and then introducing an instrument through the chest wall to visualize the intra-thoracic structures. Recent application of video cameras to thoracoscopes for high-definition magnified viewing coupled with the development of sophisticated surgical instruments and stapling devices has greatly expanded the endoscopist's ability to do increasingly more complex procedures by thoracoscopy. It was widely believed that the first to perform a documented thoracoscopy using a Nitze cystoscope in a human patient was the Swedish internist Hans Christian

Jacobaeus Thoracoscopy, the introduction of an illuminated tube through a small incision made between the ribs, was first used in 1910 for the treatment of tuberculosis. In 1882 the tubercle bacillus was discovered by Koch, and Forlanini observed that tuberculous cavities collapsed and healed after patients developed a spontaneous pneumothorax. The technique of injecting approximately 200 cc of air under pressure to create an artificial pneumothorax became a widely used technique to treat tuberculosis [1].

Jacobaeus [2], however, was able to directly visualize pleural adhesions using thoracoscopy, and described a method for cutting them to facilitate lung collapse. Closed intrapleural pneumolysis, also called the Jacobaeus operation, consisted in inserting a galvanocautery into the pleural cavity through another small opening in the chest wall and dividing the adhesions under thoracoscopic control. Thus the two-point entry technique of medical thoracoscopy was born.

After the introduction of tuberculostatic medications this surgical approach was practically abandoned until the early 1990s when advancement in fibro-optic light transmission, image display and instrumentation made video-assisted thoracoscopic surgery (VATS) possible. The improvements in video endoscopic surgical equipment and a growing enthusiasm for minimally invasive surgical approaches, brought VATS to the practice of surgery for diagnostic and therapeutic procedures. Most of these procedures required general anesthesia, a well collapse lung and are an indication for one-lung ventilation (OLV).

A variety of medical and surgical procedures are performed by VATS [3] (see Table 23.1). The patient population tends to be either very healthy, undergoing diagnostic procedures, or

TABLE 23.1. Spectrum of minimally invasive thoracic surgical procedures.

Diagnostic	
a. Pleural disease	
Biopsy, thoracentesis	
b. Staging	
Lung, pleural, esophageal cancer	
c. Parenchymal disease	
Fibrosis, solitary nodules, pneumonitis	
d. Mediastinal tumors	
Thymoma, lymphoma, sarcoma, germ cell	
e. Pericardial disease	
Pericarditis, tumors	
Therapeutic	
a. Pleural disease	
Pleurodesis, decortication	
b. Parenchymal disease	
Wedge resection, segmentectomy, lobectomy, pneumonectomy, bleb/bullae resection, lung volume reduction	
c. Cardiovascular disease	
Pericardial window, valve repair, coronary artery bypass, arrhythmia ablation	
d. Mediastinal disease	
Tumor excision, thymectomy, chylothorax	
e. Esophageal surgery	
Vagotomy, myotomy, antireflux surgery, esophagectomy	
f. Sympathectomy	
Hyperhidrosis, reflex sympathetic dystrophy	
g. Spinal surgery	

high-risk patients who are undergoing VATS to avoid the risks of thoracotomy. Patients with advanced cardiopulmonary disease, malignancies, and heavy smoking history deserve an extensive preoperative evaluation and optimization since conversion to an open procedure is always a possibility. Intraoperative monitoring in these high-risk patients should be the same as for thoracotomy.

Medical Thoracoscopy

Medical Thoracoscopy is mainly performed for diagnostic procedures. Initially it was limited to the use of rigid thoracoscope, however, with the introduction of optical fibers it was expanded to include diagnostic procedures with flexible thoracoscopy. Unlike VATS, which consist of multiple access ports, medical thoracoscopy involves the insertion of an endoscope through a single entry port into the thoracic cavity and pleural space. Medical Thoracoscopy is limited to diagnosis and biopsy of pleural disease, pleural effusions, infectious diseases, staging procedures, chemical pleurodesis, and occasionally for lung biopsy. It is often performed by the pulmonologist in the clinic rather than the operating room and is generally under local anesthesia. A small incision is made in through the lateral chest wall, and with the insertion of the instrument, fluid and biopsy specimens are easily obtained. Medical thoracoscopy has somewhat limited applications which are confined by the inability, in most cases, to perform more extensive

therapeutic procedures such as wedge resection, lobectomy or pneumonectomy.

Surgical Thoracoscopy

VATS was introduced to thoracic surgical practice in the early 1990s and entails making multiple small incisions in the chest wall, which allow the introduction of a video camera and surgical instruments into the thoracic cavity through access ports. Most commonly, it is performed by a thoracic surgeon in the operating room under general anesthesia. In more recent years surgical techniques, instruments, and video technology have improved to permit a wide variety of therapeutic procedures to be performed using VATS.

Indications: In recent years, VATS has gained increasing popularity and continues to replace many procedures that formerly required thoracotomy. Clinicians offer less invasive approaches for complex surgical treatment of lung pathology and patients are appropriately drawn to the prospect of less postoperative pain and faster recovery. Whether VATS cancer surgery, which still may involve a limited thoracotomy, carries a higher risk of local recurrence, is still unclear [4]. Some large-scale studies found no differences in overall survival between patients undergoing lobectomy and those undergoing limited resection. In fact, there is a clear difference in the treatment approach between the European schools and those of North America. There is less popularity among the European schools regarding cancer treatment through a VATS approach. This is secondary to the belief that extensive malignant tumors are best approached via open thoracotomy and proper surgical field evaluation and appropriate lymph node dissection may be limited with the VATS approach [5].

Initially, when introduced to clinical practice, VATS was limited to diagnostic procedures of short duration and limited extension. Most surgeons were unfamiliar with technique and the available equipment. Increased familiarity with thoracoscopic techniques, as with laparoscopic techniques, had enabled surgeons to perform almost any major thoracic surgical procedure in a minimally invasive manner. VATS operations can be used for all structures in the chest and are not limited to the lungs, pleura, and mediastinum.

Diagnostic Procedures

With VATS, diagnosis of pleural disease, thoracentesis, and pleural biopsy of a specific area under direct vision can be performed. In many cases this is indicated for an undiagnosed pleural effusion, in which the cytology is inconclusive. VATS for parenchymal lung pathology such as biopsy, wedge resection for solitary lung nodules or for diffuse interstitial lung disease is a common indication. In the past, such a diagnosis was possible only by subjecting the patient to an open thoracotomy, despite the associated morbidity, or the patient was treated empirically. VATS, which offers an extensive visualization of

the entire chest cavity, essentially has replaced the traditional mini-thoracotomy particularly in cases where percutaneous needle aspiration biopsy is inconclusive. Other diagnostic procedures are performed on the mediastinum for biopsy of lymph nodes not accessible via traditional mediastinoscopy such as the subcarinal lymph nodes or for mediastinal masses, either primary or metastatic. This procedure is essential when staging of the disease needs to be established. It is also useful for assessing resectability, to exclude direct invasion of the mediastinal structures. Lymphomas or germ-cell tumors that require a tissue diagnosis may benefit from a VATS approach. Diagnostic procedures involving the pericardium such as a pericardial biopsy and/or drainage of a pericardial effusion can be accomplished both for diagnosis and therapy with a VATS pericardial window.

Therapeutic Procedures

Therapeutic procedures using VATS have increased rapidly in recent years. In some institutions, the vast majority of the thoracic procedures are performed thoracoscopically.

Pleural disease can be managed by VATS including plurocentesis, pleural abrasion for recurrent pleural effusion from malignancy or pneumothorax, decortication, empyectomy, and lysis of adhesions. In the past, thoracotomy was performed for formal decortication to permit reexpansion of the lung. With VATS, thoracotomy can be avoided, particularly in the early stages of empyema. Malignant pleural effusions, particularly those with multiple loculated collections, are difficult to drain with tube thoracostomy and can be effectively treated with VATS.

Lung parenchymal disease such as wedge resection of a lesion, lobectomy or pneumonectomy can routinely be performed with VATS. These are better tolerated by the compromised patient with decreased pulmonary reserve [6]. VATS offers the opportunity to both diagnose and treat parenchymal lesions at the same time. Management of bullous disease, particularly giant bullae with significant compression of the adjacent lung, is frequently managed with VATS. Often these cases present with recurrent pneumothoraces or air-leaks associated with apical blebs. Lung volume reduction (LVR) performed by VATS is better tolerated by the patient with severe emphysema (see also Chap. 36). Resection of mediastinal masses such as thymoma or mediastinal cyst or resection of posterior mediastinal neurogenic tumors, treatment of chylothorax by ligation of the thoracic duct, bilateral sympathectomy are all possible with VATS.

A variety of esophageal procedures can be performed minimally invasively. Vagotomy, Heller myotomy, antireflux procedures, or staging of esophageal cancer are common procedures done with VATS. Finally, the dissection of the thoracic esophagus in cases of esophago-gastrectomy is increasingly performed with a combined VATS and laparotomy.

VATS sympathectomy is usually performed for hyperhidrosis or reflux sympathetic dystrophy. The sympathetic chain is visualized as it lies along the vertebral bodies.

The magnification provided by VATS facilitates the procedure, which is usually done bilaterally during the same anesthetic.

Benefits

The incisions for a VATS are usually 3–5 ports to allow for the passage of a video camera stapling device and forceps. Because the ribs are not spread, patients have lower narcotic requirements for postoperative pain, reduced shoulder dysfunction, and decreased time until return to preoperative activities. There is a reduced risk of respiratory depression, reduced risk of atelectasis due to splinting, or reduced ability to sustain deep breathing and reduction in retained secretions. A review of 1,100 VATS lobectomies with lymph node sampling or dissection in patients who had a mean age of 71.2 years demonstrated low rates of mortality (1%) and morbidity, with 84.7% of patients exhibiting no significant complications [7].

The benefits of thoracoscopy should lead to greater patient satisfaction at a lower cost (as has been the experience with laparoscopic surgery). This view is supported by Weatherford et al. in his review of the experience of thoracoscopy vs. thoracotomy at a community hospital. Weatherford compared length of stay, morbidity, mortality, operative time, length of time to extubation length of intensive care unit stay, number of days of pleural drainage and found improvements in these categories with thoracoscopy [8]. A case-control study of lobectomies found a shorter hospital stay and fewer overall complications with VATS vs. open thoracotomy but no significant decrease in postoperative atrial fibrillation [9] (see Table 23.2). Elderly patient have been shown to have fewer pulmonary, but not cardiac, complications after VATS lobectomy [10] (see Table 23.3).

Surgical Technique

VATS is performed usually in the lateral position through three to five entry ports created in the chest wall on the side

TABLE 23.2. Postlobectomy complications VATS vs. open thoracotomy.

Outcome	VATS (n=122)	Open (n=122)	p value
Length of stay (days \pm SD)	4.9 \pm 2.4	7.2 \pm 3.8	0.001
All complications	17%	28%	0.046
Atrial fibrillation	12%	16%	0.36
Prolonged air leaks	3.8%	5.7%	0.54
Pneumonitis	1.6%	4.1%	0.28

Based on data from Park et al. [9]

TABLE 23.3. Postlobectomy complications in elderly patients.

Outcome	VATS	Open	p value
Median length of stay (days)	5	6	0.001
No complications	72%	55%	0.04
Pulmonary	15%	33%	0.01
Cardiac	17%	23%	0.44

Based on data from Cattaneo et al. [10]

of the pathology (see Fig. 23.1). A video camera is inserted to allow for direct visualization of the entrance of trocars into the thorax. The lung is collapsed on the ipsilateral side by passive elastic recoil equilibrium of intrapleural and atmospheric pressure occurs through the access port. If the lung is not adequately collapsed, the surgeon is not able to appreciate the surgical field and identify a lung lesion when it is not located on the surface of the lung. Additionally, placing a stapler suture on a lung that is only partially deflated may result in inadequate closure lines which may be the source of continuous air-leak (see Fig. 23.2).

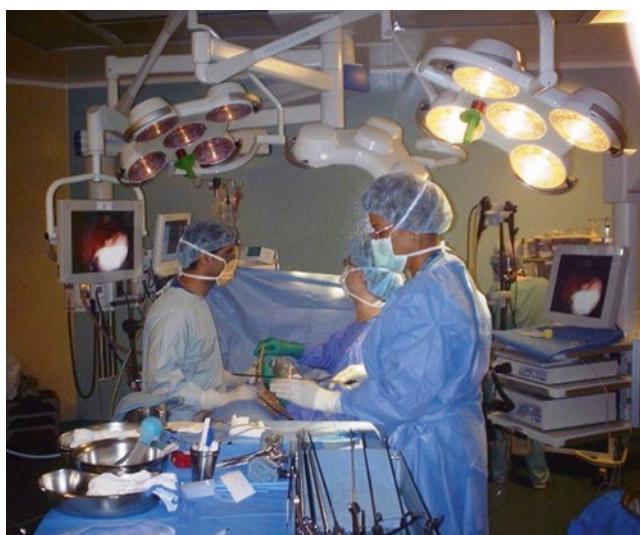


FIG. 23.1. Video-assisted thoracoscopic surgery as viewed from the foot of the operating table. A well collapsed lung on the side of surgery is necessary for any major procedure.

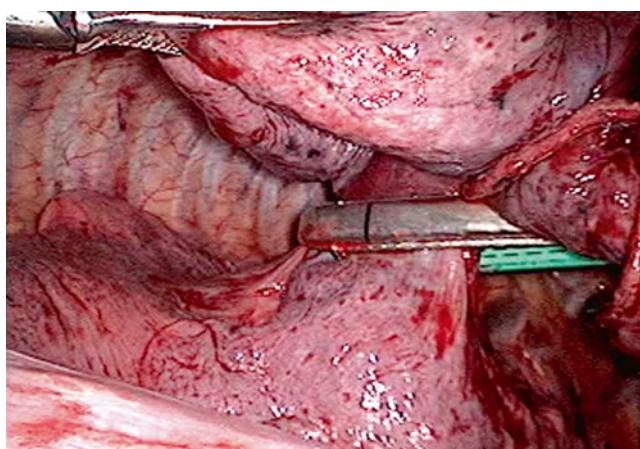


FIG. 23.2. A stapling devise is used to open the interlobar fissure as part of the initial surgical approach during a VATS lobectomy. If the lung is not well collapsed there is an increased risk of air-leaks from the staple lines.

Although rarely used in thoracoscopic procedures, unlike laparoscopic procedures, some surgeons may elect to insufflate CO_2 gas into the ipsilateral hemi-thorax to assist in collapsing the lung and breaking adhesions and to maintain the pneumothorax. There is no good evidence that a CO_2 insufflation has any benefit. Insufflation of CO_2 into the ipsilateral hemi-thorax can be associated with hemodynamic compromise and significant hypotension since the chest is a closed cavity and the increase in intra-thoracic pressure by insufflation of CO_2 will reduce venous return and cardiac output. The pressure inside the thorax must be measured and kept low. Keeping the intra-thoracic pressure below 10 cm of H_2O should minimize the negative hemodynamic effects. This is a period when communication between surgeon and anesthesiologist is crucial.

Anesthetic Management

After appropriate anesthesia and surgical evaluation, an anesthetic plan is devised to allow the patient to be safely anesthetized for the surgical procedure and to recover. Most patients find it reassuring to have a discussion with their anesthesiologist about the anesthetic and postoperative pain relief options. The choice of anesthetic technique is variable and dependent upon the wishes of the patient and the experience of the clinician. While simple diagnostic procedures can be performed under local anesthesia by infiltrating the chest wall accompanied by light sedation, more complex procedures that require sampling of tissue are best done under regional (epidural, intercostal blocks) or general anesthesia. The main disadvantage of local and regional anesthesia is that the patient is required to breathe spontaneously. While this is generally tolerated for brief periods of time, most VATS procedures today are performed under general anesthesia utilizing OLV techniques, which provides better exposure and guarantees a secure airway in the lateral decubitus position.

Each of the above techniques has its advantages and disadvantages. Decisions regarding postoperative pain relief should be made preoperatively. The management of an epidural vs. patient-controlled analgesia (PCA) vs. PRN medications given by the nurse with or without adjunctive agents is best evaluated on a daily basis by a specialist in the field of pain management. Additional considerations regarding postoperative pain management should be given to the likelihood of proceeding on to thoracotomy.

Local/Regional Anesthesia

The simplest technique is to use a local anesthetic to infiltrate the lateral thoracic wall and parietal pleura combined with appropriate sedation and supplemental oxygen. Preferably intercostal nerve blocks can be performed at the level of the incision(s) and at two interspaces above and below (see Chap. 46). Thoracic epidural anesthesia can also be used [11].

For VATS procedures under local or regional anesthesia, an ipsilateral stellate ganglion block is often performed to inhibit the cough reflex from manipulation of the hilum. To anesthetize the visceral pleura topical local anesthetics can be applied. Intravenous sedation with propofol may be needed to supplement regional nerve blocks.

For VATS performed under local or regional anesthesia with the patient breathing without assistance, partial collapse of the lung on the operated side occurs when air is allowed to enter the pleural cavity. The resulting atelectasis may provide suboptimal surgical exposure. The major disadvantage to VATS under local or regional anesthesia is that the patient must breathe spontaneously. This is usually tolerated for short periods of time, but for major VATS procedures, a general anesthetic with OLV is a better choice.

The collapse of the lung provides the surgeon with a working space, and a chest tube is placed at the conclusion of the surgery. Changes in PaO_2 , PaCO_2 , and cardiac rhythm are usually minimal when the procedure is performed using local or regional anesthesia. With local anesthesia, the spontaneous pneumothorax is usually well tolerated because the skin and chest wall form a seal around the thoracoscope and limit the degree of lung collapse. Occasionally, however, the procedure is poorly tolerated, and general anesthesia must be induced. The insertion of a double-lumen tube (DLT) with the patient in the lateral position may be difficult, in which case the patient may be temporarily placed in the supine position for the intubation.

If general anesthesia is required, a DLT is preferable to a single-lumen tube because positive-pressure ventilation via a single-lumen tube would interfere with endoscopic visualization. In addition, if pleurodesis is being performed, general anesthesia through a DLT allows for recontrolled reexpansion of the lung. A regional approach is well suited to a patient who is motivated to maintain control of their environment, a surgeon who can work gently and for a procedure that is short in duration. A benefit of regional anesthesia is that it wears off slowly over a few hours allowing for oral opioids and adjuvant analgesics to be added as needed with minimal discomfort to the patient. The risks of this approach include accidental intravenous, epidural or spinal injection with associated toxicity or cardiopulmonary embarrassment. In experienced hands, complications are rare enough to allow for the routine use of regional anesthesia for minor VATS procedures. Because the patient is not under general anesthesia and local anesthetic has only been applied to the rib cage, the patients may complain of discomfort during manipulation of lung tissue with pain referred to the shoulder. Referred shoulder pain may be difficult to differentiate from the anginal discomfort of cardiac disease.

General Anesthesia

Indications for OLV: “Lung isolation” includes the classical absolute indications for OLV, such as massive bleeding, pus,

and alveolar proteinosis or bronchopleural fistula. The goal is to protect the nondiseased contra-lateral lung from contamination. “Lung separation,” on the other hand, refers to cases with no risk of contamination to the dependent lung, and is performed primarily to improve surgical exposure such as for VATS. The inability to completely deflate the nondependent lung during VATS leads to poor surgical exposure, which in turn can jeopardize the success of the procedure, potentially requiring conversion to an open technique. Because of the increasing number of diagnostic and therapeutic procedures performed with VATS, the need to provide OLV has risen significantly. In my institution (EC), approximately 80% of the thoracic procedures either begin with or are performed entirely with VATS.

Treatment of Hypoxemia During VATS

The application of CPAP by oxygen insufflation to the nonventilated lung has traditionally been accepted as the best maneuver to treat hypoxemia during OLV [12] (see also Chap. 6). This maneuver is well accepted during open thoracotomy. Unfortunately, the application of CPAP is poorly tolerated by the surgeon during VATS because of the obstruction of the surgical field by the partially inflated lung [13] (see Fig. 23.3). Since most patients will develop atelectasis in the ventilated dependent lung during general anesthesia in the lateral position (see Fig. 23.4), recruitment maneuvers [14], and the application of PEEP to the ventilated-lung are useful in the majority of patients, except those with severe obstructive lung disease [15] (see Fig. 23.5). A useful method of improving oxygenation during OLV for VATS is the bronchoscopic-guided insufflation of oxygen into segments of the nondependent lung remote to the site of surgery [16] (see Chap. 6, Fig. 6.11).

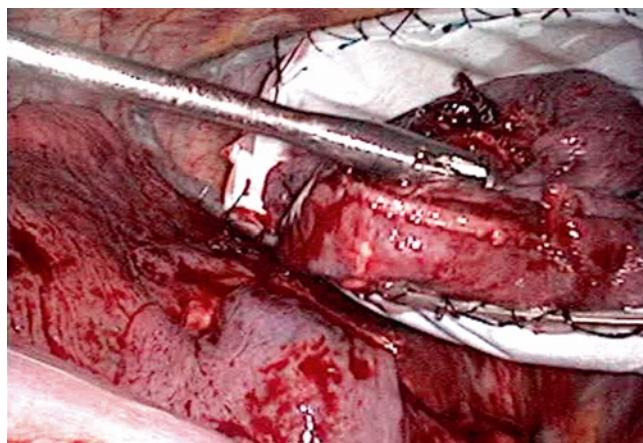


FIG. 23.3. During a VATS lobectomy the excised lobe is placed in a retrieval bag before being removed through a small chest wall incision. Good collapse of the operative lung is required for the surgeon to perform this operation.

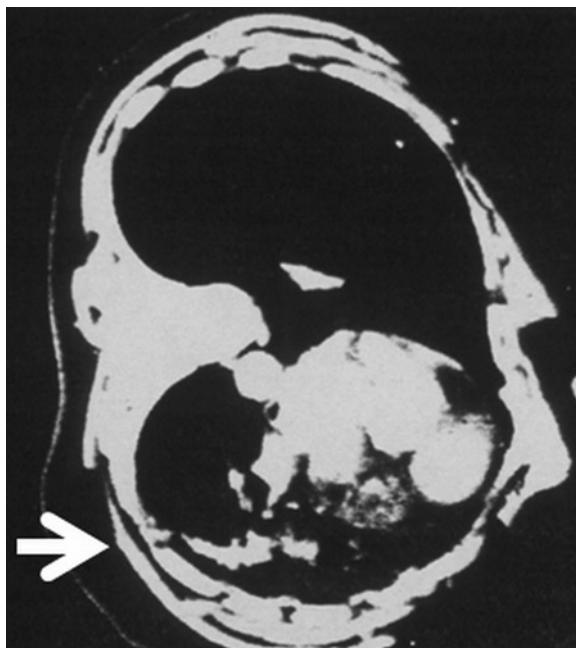


FIG. 23.4. Chest CT scan during general anesthesia in the lateral position. The white arrow points to a plaque of atelectasis in the dependent lung. Most patients develop atelectasis in the dependent lung during anesthesia.

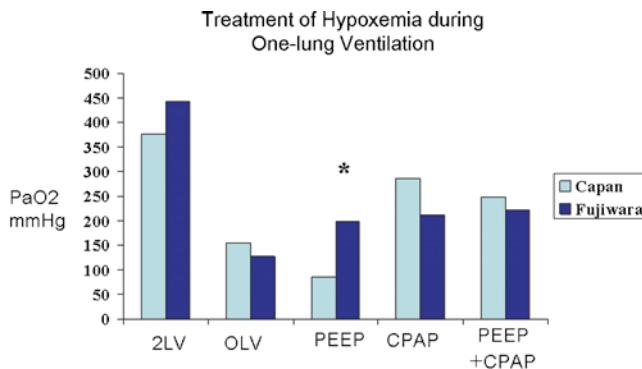


FIG. 23.5. A comparison of the effects of PEEP and CPAP on oxygenation during one-lung ventilation in patients with COPD (Capan) vs. normal pulmonary function (Fujiwara). PEEP improves PaO₂ for most patients with normal pulmonary function during OLV (asterisk significant improvement $p < 0.05$) but decreases PaO₂ in patients with COPD (based on data from Thomsen [13] and Fujiwara et al. [15]).

Improving Lung Collapse During VATS

Since a collapsed immobile lung on the side of surgery is fundamental to VATS for major pulmonary resections, one of the Anesthesiologists responsibilities is to facilitate collapse of the nonventilated lung. There are three basic manuvers that will increase the rate of lung collapse.

1. Eliminate all nitrogen from the operative lung prior to the initiation of lung collapse. The poorlysoluble nitrogen in air delays collapse in nonventilated alveoli. Although

Passive Paradoxical Gas Exchange in the Non-Ventilated Lung during Closed-Chest One-Lung Ventilation

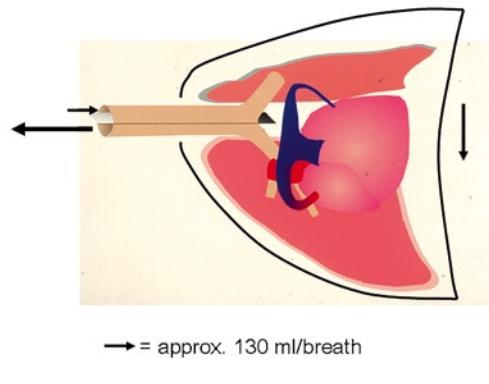


FIG. 23.6. Passive paradoxical gas exchange occurs in the nonventilated lung during OLV if the chest is closed. As the mediastinum falls during exhalation of the ventilated lung, the resultant negative pressure in the nonventilated hemi-thorax entrains room air into the nonventilated lung if the lumen of the DLT is open to atmosphere. This air is then expired during the inspiration phase of the ventilated lung. The passive tidal volumes depend on the size of the patient and cease once the initial VATS port allows atmospheric pressure to equilibrate in the nonventilated hemi thorax (based on data from Pfitzner et al. [18]).

the use of air–oxygen mixtures are desirable to prevent the development of atelectasis in the ventilated lung during one-lung anesthesia, if air is present in the nonventilated lung at the start of OLV it will delay collapse [17] (see Chap. 6, Fig. 6.6). It is best to ventilate with a FiO₂ of 1.0 for a period of 3–5 min immediately prior to the start of OLV to de-nitrogenate the operative lung. After a recruitment maneuver of the ventilated dependent lung, air can then be reintroduced to the gas mixture after the start of OLV as tolerated, according to the arterial oxygen saturation.

2. Avoid entrainment of room air into the nonventilated lung during closed-chest OLV. Many anesthesiologists will begin OLV as soon as possible to encourage lung collapse prior to the start of surgery. However during closed-chest OLV, if the lumen of the DLT to the nonventilated lung is open to atmosphere, passive paradoxical ventilation of the nonventilated lung will occur (inspiration during the expiratory phase of the ventilated lung) and air will be drawn into the nonventilated lung delaying collapse (see Fig. 23.6). It has been shown that these passive tidal volumes are approximately 130 mL/breath [18] which far exceeds the dead-space of one side of a DLT (10–15 mL). These passive tidal volumes cease as soon as atmospheric pressure is allowed into the operative hemi-thorax.
3. Apply suction to the lumen of the DLT or bronchial blocker to the nonventilated lung at the start of OLV. Low suction (-20 cm H₂O) improves the rate of lung collapse for both open thoracotomy and VATS [19] (see Fig. 23.7). It is not clear whether the effect of suction is due to the negative pressure or simply due to a suction catheter preventing passive entrainment of air into the nonventilated lung (see Fig. 23.8).

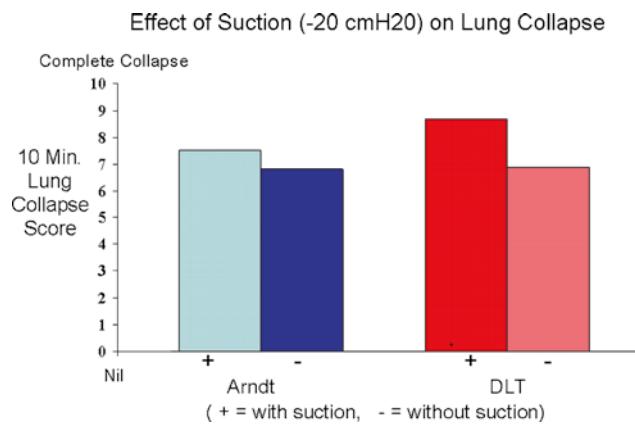


FIG. 23.7. The application of low suction to the channel of a bronchial blocker (in this case the Arndt blocker) or to the lumen of the DLT to the nonventilated lung significantly improves the speed of lung collapse measured both 10 min (shown here) and 20 min after the start of OLV (based on data from Narayanaswamy et al. [19]).



FIG. 23.8. Photograph of suction being applied via a catheter to the tracheal lumen of a left-sided DLT during a right-sided VATS procedure. Low suction (-20 cm H₂O) should be applied from the start of OLV until the nonventilated lung is completely collapsed.

Verifying Patency of Remaining Bronchi

During open thoracotomy for lobectomy, to ensure that the patency of a bronchus to a remaining lobe has not been compromised, the surgeon will often ask the anesthesiologist to temporarily reinflate the nonventilated lung after the stapling device has occluded the bronchus to the operative lobe or segment, just before the desired bronchus is cut and stapled.

Reinflation of the ipsilateral remaining lobe(s) ensures the patency of their bronchi. However, during a VATS resection, this maneuver impairs the surgeon's ability to visualize the surgical field and to proceed with the resection. To avoid this potential for compromise of noninvolved bronchi during VATS the anesthesiologist may be asked to perform fiberoptic bronchoscopy at this stage to ensure that the bronchi to the remaining ipsilateral lobe(s) is/are patent (see Fig. 23.9a, b). To perform this, the anesthesiologist needs a detailed knowledge endoscopic bronchial anatomy (see Chap. 16).

Lung Isolation

The use of DLT has classically been considered the “gold standard” for achieving OLV. Proper position of the DLT or endobronchial blocker is often confirmed in the supine position, but it is when the patient has been placed in the lateral decubitus position that matters most since the surgery will take place in that position and dislocation during position changes are not uncommon. A study conducted by Narayanaswamy et al. [19] showed in 104 patients undergoing left-sided lung surgery that, in regards to quality of surgical exposure, there was no difference between the use of bronchial blockers (Arndt wireguided, Cohen Flexi-tip, Fuji Uni-blocker) and a left-sided DLT. However, significant differences were found favoring the use of DLTs with regards to time to initial lung deflation and amount of repositioning required after initial placement of the lung isolation device. Since most VATS procedures require lung separation and not isolation, the insertion of a bronchial blocker to obtain OLV is an attractive alternative to a DLT, especially since multiple intubations of the trachea will not be necessary when using a bronchial blocker. Additionally, a difficult intubation is even more difficult much when using a DLT.

Management of One-Lung Ventilation

Peak airway pressure, delivered tidal volume (spirometry) and the wave-form of the capnogram, should be inspected to identify obstruction or reduced end-tidal carbon dioxide tension from inadequate gas exchange subsequent to DLT malposition. A peak airway pressure of up to 35 cm H₂O during OLV is acceptable. A sudden increase in the peak airway pressure (during volume-controlled ventilation) may be from DLT or endobronchial blocker dislocation. These tube or blocker movements are often a consequence of surgical manipulation. During pressure-controlled ventilation, this will present as a fall in tidal volume. When OLV is required, a FiO₂ of 1.0 provides the greatest margin of safety against hypoxemia. When using a FiO₂ of 1.0, assuming a typical HPV response, the expected PaO₂ during OLV should be between 150 and 210 mmHg. I typically ventilate OLV patients with a tidal volume of 6–7 mL/kg, PEEP 5 cm H₂O, and at a respiratory rate sufficient to maintain a PaCO₂ of 35 ± 3 mmHg. Following the initiation of OLV, PaO₂ can continue to decrease for up

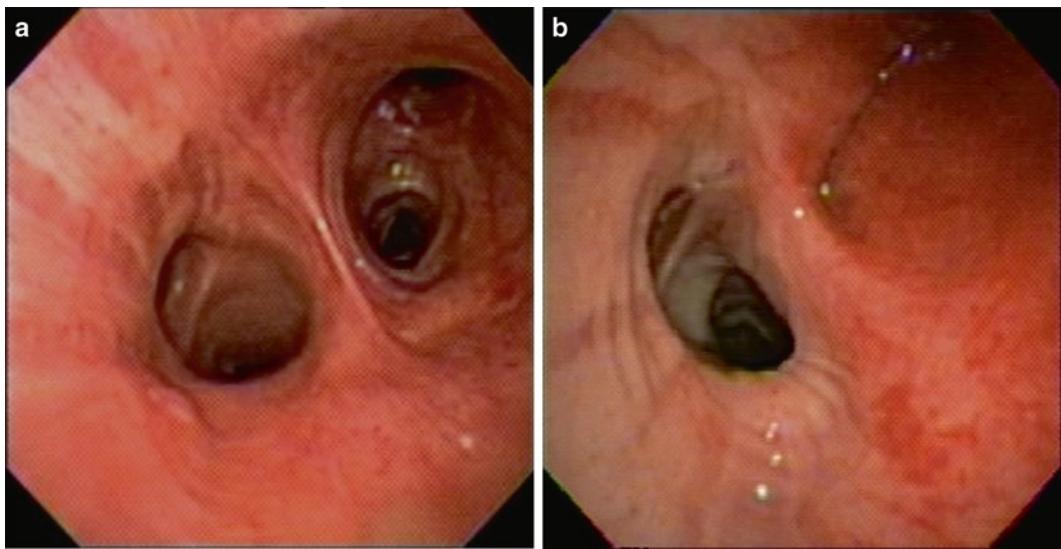


FIG. 23.9. (a) Normal anatomy of the secondary carina of the left lung as seen during fiberoptic bronchoscopy during VATS lobectomy. The left upper lobe orifice is at the upper right. The posterior wall of the mainstem bronchus is identified by the longitudinal elastic bundles, seen at 9 o'clock, which extend into the left lower lobe. (b) A surgical stapler has been applied to the left upper lobe bronchus. The anesthesiologist is asked to ensure that the bronchus to the left lower lobe remains patent, as seen in the photograph, prior to firing the stapler.

to 45 min; hence, a pulse oximeter is indispensable. Should hypoxia occur, proper positioning of the DLT should be reconfirmed using fiberoptic bronchoscopy.

Other Anesthetic Considerations for VATS

In addition to the usual complications related to intra-thoracic surgery and anesthesia, thorascopic procedures can be associated with massive hemorrhage and decreased inability to control large blood vessels. Maintaining stable hemodynamics can present a challenge until the surgeon gets control of the source of bleeding which may require conversion to an open thoracotomy. Therefore, large bore intravenous catheters are even more critical for VATS procedures than open thoracotomy where the hilar blood vessels can be controlled easier. Bleeding can be from placement of trocars into the lung or great vessels.

A false assumption that is made by patients coming for minimal invasive surgery is that the perioperative risk will also be “minimal.” VATS is frequently described to the patient and their family as a simple entry into the chest. While VATS is associated with improved healing, lung function and shorter hospital length of stay, by no means should one be lured into thinking that the procedure is any less invasive than an open thoracotomy. Diagnostic VATS procedures are being increasingly performed on ASA III–IV patients, who historically would have been classified as inoperable using an open approach. An example would be a patient on the cardiac transplant list that needs a pretransplant tissue diagnosis of a lung lesion seen on a preoperative chest X-ray. Consequently, very ill patients requiring flawless lung separation techniques, who expect an uneventful perioperative course, pose an increased stress for the anesthesia team.

Postoperative Pain Management

Extensive discussion of the management of postthoracotomy pain can be found in Chap. 46. A commonly cited advantage of VATS when compared to open thoracotomy is a reduction in postoperative pain. While this is true in a relative sense, VATS procedures are still associated with a significant amount of postoperative pain, that is not only disturbing to patients, but may be associated with pain-related morbidities and prolonged hospital stays. The preponderance of literature suggests that VATS lung resection is associated with decreased postoperative pain compared with conventional thoracotomy. Sugiura and colleagues found a reduced duration of epidural catheter use, less narcotic use, decreased frequency of analgesic administration, and possibly a lower incidence of postthoracotomy pain syndrome in patients undergoing VATS compared with those undergoing thoracotomy [20].

Thoracic epidural analgesia has a long track-record of efficacy and safety and is considered by many anesthesiologists the gold standard in pain relief during the postoperative period for the thoracic patient. While other forms of postoperative analgesia are possible, many are associated with unwanted side effects. Systemic opioids are respiratory depressive and inhibit the cough reflex. Nonsteroidal antiinflammatory medication can inhibit coagulation and in isolation do not suffice to control the immediate postoperative pain experienced by this patient population. The utilization of paravertebral blocks has shown promise as an alternative to epidural analgesia.

The control of postoperative pain in patients after intra-thoracic surgery is critical to the rehabilitation of their respiratory function. Postoperative pain in the chest wall can cause splinting which will impair coughing, deep breathing leading to

retention of secretions and a decrease in FRC. These problems have been shown to be a source of great morbidity and should be managed aggressively. The options for postoperative pain management should begin preoperatively and not postoperatively. A frank discussion with the patient will allow the patient to discuss their fears of anesthesia and postoperative pain. Pain control options include: Cognitive/behavioral (i.e., relaxation, distraction and imagery techniques), Intravenous administration of opioids and adjuvant agents (i.e., nonsteroidal antiinflammatory drugs, tri-cyclic agents) on an “around the clock” and or PRN basis, PCA intravenous pumps, neuraxial (epidural, intrathecal) agents (local anesthetics, opioids, ketamine, clonidine, alpha agonists), intermittent neural blockade (with local anesthetics, cryoprobe, neurolytic agents) or continuous neural blockade (with an intrapleural catheter), physical application of hot and cold compresses or TENS (transcutaneous electrical nerve stimulation). The surgical technique plays a very important part in the level of pain the patient will have postoperatively. There should be less pain associated with a VATS vs. open thoracotomy since there is less chest wall muscle damage. Controversy exists whether thoracic epidural analgesia is necessary for procedures performed with VATS since the pain experience is less dominated by the incisional component, compared to a thoracotomy. Thoracoscopy pain reflects more the visceral, pleural and diaphragmatic nociceptive components. Multimodal techniques involving a combination of intraoperative intercostal nerve blocks, pre and postoperative oral antiinflammatories and postoperative intravenous patient-controlled opioid analgesia is a common strategy for the majority of VATS patients in many centers. Thoracic epidural may be reserved for patients with severe pulmonary dysfunction who are at a high risk for postoperative respiratory complications.

Clinical Case Discussion

A 67-year-old-male with a right upper lobe nonsmall cell lung tumor is scheduled for VATS right upper lobectomy (see Fig. 23.10). He has COPD, preoperative FEV1 is 57% predicted and DLCO is 60%. No other comorbidities. After intravenous induction of anesthesia he is intubated with a left DLT. After turning the patient to the left lateral position and confirming the position of the DLT with fiberoptic bronchoscopy, one-lung anesthesia is begun with sevoflurane (1MAC) and a FiO_2 of 1.0, pressure-control ventilation, tidal volume 6 mL/kg, resp. rate 12/min. When the surgeon places the VATS camera in the right chest the lung is not completely collapsed. What can be done to improve lung collapse?

Answer: The position of the DLT should be reconfirmed with bronchoscopy. The adequacy of lung isolation should be confirmed by verifying that the inspired and expired tidal volumes of the left lung match using side-stream spirometry (the expired tidal volume is often a small percentage lower than the inspired volume due to the greater uptake of oxygen than the production of CO_2). The use of FiO_2 1.0 to the operative lung prior to the initiation of OLV will increase the rate of

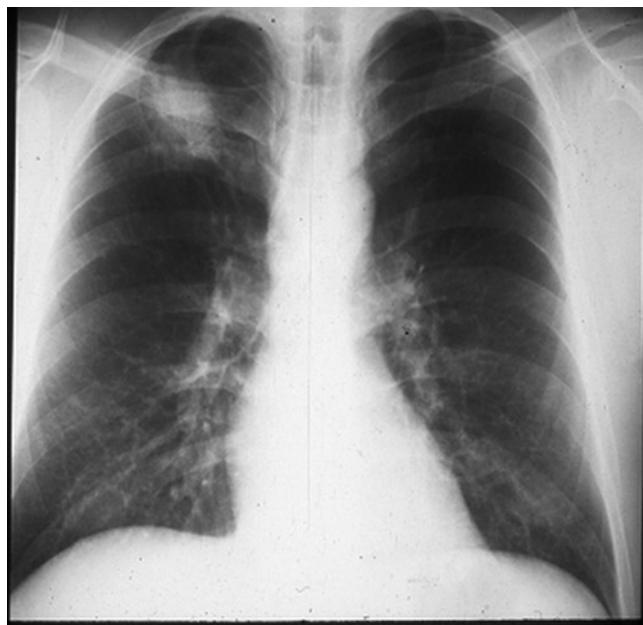


FIG. 23.10. Chest X-ray of a patient with a right upper lobe nonsmall cell lung cancer scheduled for VATS lobectomy. The patient has moderate COPD as evidenced by the hyperinflation of the lungs and the narrow cardiac silhouette.

lung collapse and a low suction (20 cm H_2O) applied to the nonventilated lung will also speed collapse (see text).

With the onset of OLV the arterial oxygen saturation begins to slowly decrease. All other vital signs are stable: HR 78, BP 130/82 and PetCO_2 32 mmHg. After 20 min of surgery the SpO_2 has fallen to 89% and continues to decline. What is the most appropriate next step?

Answer: After reconfirming the FiO_2 and the correct position of the DLT with bronchoscopy, a recruitment maneuver of the left lung is performed and PEEP 5 cm H_2O is added to the left lung. In spite of these therapies the SpO_2 continues to fall and is now 87%. The Anesthesiologist suggests applying CPAP to the operative left lung. The Surgeon is adamant that he/she will not be able to complete the operation as a VATS procedure if CPAP is necessary and will have to convert to an open thoracotomy. Is there any other therapy that can improve oxygenation and will not interfere with surgical exposure?

Answer: Guided insufflation of oxygen at 5 L/min into the basilar segments of the right lower lobe is performed for 30 s. via the suction channel of the fiberoptic bronchoscope while the surgeon monitors the insufflation using the VATS camera (see Chap. 6, Fig. 6.11). After partial reinflation of the anterior and lateral basal segments of the right lower lobe the SpO_2 increases to 93% and surgery continues. The bronchoscopic segmental insufflation needed to be repeated once again 20 min later when the SpO_2 fell to <90%. Surgery was completed without complication or conversion to open thoracotomy. Management of hypoxemia during VATS procedures is outlined in Table 23.4.

TABLE 23.4. Management of hypoxemia during VATS.

Severe or acute desaturation

Resume two-lung ventilation

Gradual desaturation

1. Assure $\text{FiO}_2 = 1.0$
2. Check double-lumen tube or bronchial blocker placement with fiberoptic bronchoscopy
3. Optimize cardiac output
4. Recruitment maneuver of the ventilated lung
5. Apply PEEP 5 cm H_2O to ventilated lung (except moderate-severe COPD patients)
6. Partial ventilation of the nonventilated lung
 - (i) Segmental reinflation (with fiberoptic bronchoscopy)
 - (ii) High frequency jet ventilation

9. Park BJ, Zhang H, Rusch VW, Amar D. Video-assisted thoracic surgery does not reduce the incidence of postoperative atrial fibrillation after pulmonary lobectomy. *J Thorac Cardiovasc Surg*. 2007;133:775–9.
10. Cattaneo SM, Park BJ, Wilton AS, et al. Use of video-assisted thoracic surgery for lobectomy in the elderly results in fewer complications. *Ann Thorac Surg*. 2008;85:231–6.
11. Williams A, Kay J. Thoracic epidural anesthesia for thoracoscopy, rib resection, and thoracotomy in a patient with a bronchopleural fistula postpneumonectomy. *Anesthesiology*. 2000;92:1482–4.
12. Capan LM, Turndorf H, Patel C, et al. Optimization of arterial oxygenation during one-lung anesthesia. *Anesth Analg*. 1980;59:847–51.
13. Thomsen RW. Mediastinoscopy and video-assisted thoracoscopic surgery: anesthetic pitfalls and complications. *Sem Cardiothorac Vasc Anesth*. 2008;12:128–32.
14. Tusman G, Bohm SH, Sipmann FS, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. *Anesth Analg*. 2004;98:1604–9.
15. Fujiwara M, Abe K, Mashimo T. The effect of positive end-expiratory pressure and continuous positive airway pressure on the oxygenation and shunt fraction during one-lung ventilation with propofol anesthesia. *J Clin Anesth*. 2001;13:473–7.
16. Ku C-M, Slinger P, Waddell T. A novel method of treating hypoxemia during one-lung ventilation for thoracoscopic surgery. *J Cardiothorac Vasc Anesth*. 2009;23:850–2.
17. Ko R, McRae K, Darling G, et al. The use of air in the inspired gas mixture during two-lung ventilation delays lung collapse during one-lung ventilation. *Anesth Analg*. 2009;108:1092–6.
18. Pfitzner J, Peacock MJ, McAleer PT. Gas movement in the non-ventilated lung at the onset of single-lung ventilation for video-assisted thoracoscopy. *Anaesthesia*. 2000;54:437–43.
19. Narayanaswamy M, McRae K, Slinger P, et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. *Anesth Analg*. 2009;108:1097–101.
20. Sugiura H, Morikawa T, Kaji M, et al. Long-term benefits for the quality of life after video-assisted thoracoscopic lobectomy in patients with lung cancer. *Surg Laparosc Endosc*. 1999;9:403–8.

References

1. Sakula A. Carlo Forlanini, inventor of artificial pneumothorax for treatment of pulmonary tuberculosis. *Thorax*. 1983;38:326–32.
2. Jacobaeus HC. The cauterization of adhesions in artificial pneumothorax treatment of pulmonary tuberculosis under thoracoscopic control. *Proc R Soc Med*. 1923;16:45–62.
3. Fischer GW, Cohen E. An update on anesthesia for thoracoscopic surgery. *Curr Opin Anaesthesiol*. 2010;23:7–11.
4. Shiraishi T, Shirakusa T, Iwasaki A, et al. Video-assisted thoracoscopic surgery (VATS) segmentectomy for small peripheral lung cancers. *Surg Endosc*. 2004;18:1657–62.
5. Shaw JP, Dembitzer FR, Wisnivesky JP, Little VR, Weiser TS, Yun J, et al. Video-assisted thoracoscopic lobectomy: state of the art and future directions. *Ann Thorac Surg*. 2008;85:S705–9.
6. Demmy TL, Curtis JJ. Minimally invasive lobectomy directed toward frail and high-risk patients: a case-control study. *Ann Thorac Surg*. 1999;68:194–200.
7. McKenna Jr RJ, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1, 100 cases. *Ann Thorac Surg*. 2006;81:421–5.
8. Weatherford DA, Stephenson JE, Taylor SM, Blackhurst D. Thoracoscopy versus thoracotomy: indications and advantages. *Am Surg*. 1995;61:83–6.

Anesthesia for Patients with End-Stage Lung Disease

Martin Ma and Peter Slinger

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Key Points

- Preoperative optimization with pulmonary rehabilitation, smoking cessation, and education can improve surgical outcomes in patients with end-stage lung disease (ESLD).
- ESLD is associated with a high incidence of pulmonary hypertension and right ventricular dysfunction. The anesthetic goals for these patients include optimizing preload, maintaining a low normal heart rate, maintaining contractility, decreasing pulmonary vascular resistance, and ensuring systemic pressures are greater than pulmonary pressures.
- Compared with general anesthesia, regional anesthesia and analgesia may reduce the risk of pulmonary complications and perioperative morbidity.
- Even mild pulmonary insults will be poorly tolerated by patients with ESLD. Ventilation strategies that utilize low tidal volumes and low airway pressures may reduce the risk of volutrauma, barotrauma, and acute lung injury.
- Intraoperative management can facilitate early recovery and early tracheal extubation after general anesthesia. Short-acting anesthetic agents are recommended. As elimination of inhalational agents is impaired by ESLD, total intravenous anesthesia (TIVA) may be preferred. Maintenance of normothermia will avoid increases in ventilatory demand associated with postoperative shivering.
- Effective postoperative analgesia is essential in patients with ESLD. Regional analgesia is preferred over parenteral opioid analgesics. Adjuvant pain medications which have an opioid-sparing effect should be used.
- Chronic obstructive pulmonary disease is a common cause of ESLD. Severe airflow obstruction results in a high risk of air-trapping, pneumothorax, and dynamic hyperinflation. In addition to aggressive bronchodilation, ventilation with low inspiratory:expiratory ratios (1:3 to 1:4.5) and low respiratory rates (6–10/min) will optimize expiratory airflow.
- Cystic fibrosis is a multisystemic disease that results in abnormally viscous secretions. Inability to clear pulmonary

secretions results in airflow obstruction and chronic infection. Management focuses on improving sputum clearance and minimizing airway obstruction.

- The interstitial lung diseases cause lung restriction and are characterized by chronic inflammation and fibrosis. Ventilation strategies that minimize tidal volume and airway pressures should be used.

Introduction

Providing a safe anesthetic for patients with end-stage lung disease (ESLD) is a challenge. Postoperative pulmonary complications are poorly tolerated in this group of patients and can result in significant morbidity and mortality. Ideally, efforts to minimize this risk begin in the preoperative period with patient education, pulmonary rehabilitation programs, and smoking cessation counseling. Although this is not always possible, participation in these programs can reduce perioperative complications. Intraoperatively, problems may include inadequate oxygenation and ventilation, as well as barotrauma, volutrauma, and acute lung injury (ALI). In this high-risk patient population, an anesthetic technique that facilitates early recovery and tracheal extubation is also of key importance. Optimal perioperative management of patients with ESLD requires a multidisciplinary medical team approach that includes respirologists, surgeons, nurses, physiotherapists, respiratory therapists, and of course anesthesiologists. This chapter begins with an overview of the management considerations that are applicable to all patients with ESLD. This discussion is summarized in Table 24.1. Specific considerations for the most common causes of ESLD including chronic obstructive lung disease (COPD), cystic fibrosis (CF), and interstitial lung disease (ILD) are then outlined.

TABLE 24.1. Summary of anesthetic management for patients with end-stage lung disease (ESLD).

Optimization	Enroll patients in pulmonary rehabilitation Encourage smoking cessation Educate patients on postoperative chest physiotherapy Ensure preoperative use of routine bronchodilators
Anesthesia	Patients may have pulmonary hypertension. These goals are summarized in Table 24.4 Regional anesthesia and analgesia will minimize the risk of postoperative pulmonary complications Emergence is more predictable with short-acting agents and total intravenous anesthesia (TIVA) Maintain normothermia
Ventilation	Avoid prophylactic insertion of nasogastric tubes Use low tidal volume ventilation (~ 6 mL/kg) Maintain airway pressures as low as possible
Postoperative care	Patients will require care in a monitored setting postoperatively (e.g., step down unit, intensive care unit) Minimize opioid use while maximizing nonopioid pain medications

Preoperative Optimization

Pulmonary Rehabilitation

In patients with ESLD, pulmonary rehabilitation programs can improve overall functional status. The primary focus of this comprehensive intervention is the reversal of peripheral muscle deconditioning through both aerobic and strength training. Patient education, improved nutrition, and psychosocial support are also key elements. Improved muscle function results in greater physical stamina. For any given activity this translates into decreased lactic acid production, decreased carbon dioxide (CO_2) production, and thus, decreased ventilatory demand [1, 2]. Although this benefits all patients with ESLD, it is particularly relevant to those with COPD in whom hyperventilation causes inadequate expiratory time, dynamic hyperinflation, and worsened dyspnea. The educational component of pulmonary rehabilitation aims to improve the patient's understanding of the disease and its management. Common themes include smoking cessation, the early detection and treatment of pulmonary exacerbations, the role of exercise in improving function, and promoting compliance with therapy. ESLD is often associated with poor nutritional status which results in muscle catabolism. In and of itself, aggressive nutritional support in patients with advanced lung disease has not led to clinically relevant improvements in functional outcome [3–5]. When used in conjunction with exercise, nutritional support may improve lean muscle mass function and improve exercise performance [6].

After studying most extensively in patients with COPD, pulmonary rehabilitation programs have been shown to significantly improve exercise capacity and health-related quality of life while reducing the severity of dyspnea [5, 6]. In a metaanalysis of 18 studies by Cambach et al. [7], pulmonary rehabilitation significantly improved maximal exercise capacity, endurance time, and walking distance of patients with COPD. In a more recent meta-analysis of 31 randomized controlled trials, the mean distance walked by patients with COPD in 6 min increased by 48 m following training. This approximated the estimated minimum clinically significant difference of 50 m [8]. In both reviews, a significant improvement in quality of life measures of dyspnea, fatigue, emotion, and patient control over disease were observed [7, 8].

Although the impact of pulmonary rehabilitation is less well studied for other forms of ESLD, current evidence suggests that it is beneficial. In a study comparing 309 patients with COPD and 113 with non-COPD lung disease, a 6-week rehabilitation program resulted in similar statistically significant improvements in exercise tolerance and quality of life markers [9]. A similar outcome was observed in a study specifically comparing 26 patients with restrictive lung disease to 40 patients with COPD [10]. In a small study of 25 patients with pulmonary hypertension, an exercise program reduced New York Heart Association dyspnea scores and improved 6-min walk test results [11]. For CF patients, exercise training has been associated with a reduction in lactate levels and

heart rate [12]. Current evidence-based guidelines strongly recommend pulmonary rehabilitation programs for patients with COPD and other causes of ESLD [6].

In the preoperative setting, pulmonary rehabilitation is mandatory for patients undergoing lung volume reduction surgery (LVRS) and lung transplantation. For these high-risk procedures, successful completion of pulmonary rehabilitation is used not only as a marker for patient motivation and therapy compliance, but also as a risk assessment tool. For example, the National Emphysema Treatment Trial (NETT) found that patients with primarily upper lobe emphysema and low maximal workload after rehabilitation benefited from LVRS. In comparison, patients with non-upper lobe emphysema and high maximal workload following rehabilitation have higher mortality rates with LVRS than conservative management with medical therapy only [13].

There is a growing interest in establishing whether preoperative pulmonary rehabilitation may play a role in either (1) improving exercise reserve sufficiently to enable borderline operative candidates to undergo surgery, or (2) improving perioperative outcome. Patient suitability for lung resection is commonly based upon three factors: respiratory mechanics, lung parenchymal function, and cardio-pulmonary reserve. While lung function is relatively fixed, cardio-pulmonary reserve can be improved. In a small pilot study, eight COPD patients with resectable lung cancers were denied surgery as a result of poor pulmonary function (mean preoperative forced expiratory volume in 1 s predicted = 40%). Following 4 weeks of pulmonary rehabilitation, all eight patients successfully had a lobectomy [14]. With respect to improving patient outcome, the role of preoperative pulmonary rehabilitation has been examined in one small study of 45 patients with COPD undergoing coronary artery bypass grafting. Pulmonary rehabilitation led to significantly lower postoperative ventilation times, postoperative complications, and hospital length of stay [15]. Although the preoperative role of pulmonary rehabilitation appears promising, there is currently very little clinical evidence to support or refute its use.

Smoking Cessation

The link between smoking and increased perioperative morbidity is well established in the literature. From an anesthesiologist's perspective, smoking increases the relative risk of postoperative pulmonary complications by up to six times [16]. A common concern is the increased risk of laryngospasm and bronchospasm. High levels of carbon monoxide limit the ability of hemoglobin to bind and transport oxygen, predisposing surgical patients to an increased risk of hypoxia. Smoking increases airway mucous production and impairs ciliary function resulting in poor sputum clearance. This, in combination with smoke-induced impairment of immune function, increases the likelihood of developing postoperative pneumonia. The long-term pulmonary consequence of smoking is worsening airway obstruction as measured by the forced expired volume in 1 s (FEV₁). Although cessation will not reverse the degree of airway obstruction caused by smoking, it does reduce the rate at which FEV₁ subsequently declines (Fig. 24.1). Nicotine causes direct coronary vasoconstriction as well as an increase in the rate-pressure product. This contributes to the observation that smokers with no history of coronary artery disease have significantly more episodes of ST segment depression during surgery than nonsmokers [17]. Other concerns include impaired wound healing and perioperative venous thrombosis secondary to a procoagulant state caused by nicotine. The reversible effects of smoking are summarized in Table 24.2. Given the potential perioperative cardio-respiratory complications of smoking, preoperative cessation is important for patients with ESLD.

Although the long-term benefits of smoking cessation are undisputed, its timing before surgery is controversial. A clear reduction in pulmonary complications occurs when smoking cessation occurs 2 months prior to surgery. In a study of 200 patients undergoing coronary artery bypass surgery, Warner et al. examined the rates of pulmonary complications in relation to timing of smoking cessation. The pulmonary

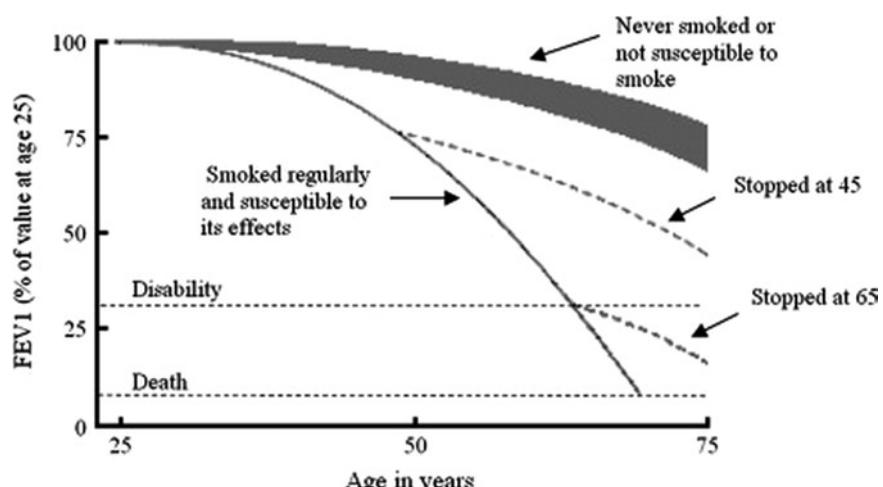


FIG. 24.1. Decline in FEV₁ with age and smoking (reprinted from Kemp et al. [84]. © 2009 with permission from Elsevier).

TABLE 24.2. Reversible effects of smoking.

Respiratory		
• ↑ Carbon monoxide		↑ Risk of hypoxia
• ↑ Mucous production		↑ Risk of pulmonary infections
• ↓ Ciliary function		
• ↓ Immune function		
• ↑ Airway reactivity		↑ Risk of bronchospasm
Cardiac		
• ↑ Rate-pressure product		
• ↑ Myocardial O ₂ consumption		
• Coronary vasoconstriction		↑ Risk of ischemia
Hematologic		
• ↓ Macrophage function		
• ↑ Platelet aggregation		
• ↑ Coagulation		↓ Immune function
Impaired wound healing		↑ Risk of thrombosis

complication rates were 33% for current smokers, 14.5% for ex-smokers who quit >2 months preoperatively, 11.9% for ex-smokers who quit >6 months preoperatively, and 11.1% for nonsmokers. Interestingly, however, if patients stopped smoking less than 2 months before surgery, the incidence of perioperative complications (57.1%) was actually higher than patients who continued to smoke [18]. A similar trend has also been observed by Nakagawa et al. [19]. In another study, patients who reduced but did not stop cigarette use had a 14.2 greater relative risk of pulmonary complications than patients who continued their usual cigarette consumption [16]. Why complication rates may rise when smoking is reduced or stopped less than 2 months before surgery remains unclear. More recently, a study of 300 patients undergoing thoracotomy for lung cancer resection found no evidence of a paradoxical increase in pulmonary complications among those who quit smoking within 2 months of surgery [20]. The conflicting data results in a dilemma. Because anesthesiologists typically meet patients a few weeks or days prior to surgery, should we advise smokers to reduce or stop cigarette use? For many physicians, to deliberately avoid an opportunity to counsel against smoking would seem counterintuitive. At the very least, patients should probably be advised to stop smoking 12–24 h prior to surgery to minimize the concentration and harmful effects of carbon monoxide and nicotine.

Effective interventions to assist patients who wish to quit smoking include medical advice and pharmacotherapy such as nicotine replacement, bupropion, and clonidine. In one study, 117 smokers scheduled for elective orthopedic or general surgery were randomized to either the smoking cessation intervention group or the control group. Beginning 4 weeks prior to surgery, and ending 4 weeks after surgery, the intervention group received weekly counseling and free nicotine replacement therapy. The intervention group was significantly more likely to not smoke throughout the perioperative period (36% vs. 2%; $P<0.001$) and remain abstinent 1 year after (33% vs. 15%; $P=0.03$) [21].

Medical Optimization

To minimize the risk of perioperative pulmonary complications, care must be taken to ensure that patients with ESLD are medically optimized prior to elective surgery. Bronchospasm and difficulty in clearing sputum are common problems in patients with COPD, bronchiectasis, and CF, and may contribute to the development of hypoxia, atelectasis, and pneumonia. This risk may be decreased with the use of maximal bronchodilator and inhaled glucocorticoid therapy in the immediate preoperative period. In patients with ineffective sputum clearance, chest physiotherapy is warranted. While this recommendation makes intuitive sense, there are no controlled trials that prove efficacy [22, 23]. During an acute exacerbation, patients may benefit from aggressive antibiotic and systemic steroid therapy [23–25]. The development of pulmonary hypertension is common among all patients with ESLD. Appropriate medical therapy to minimize pulmonary artery pressure (PAP) and improve right ventricular function should be instituted as needed prior to surgery.

Chest Physiotherapy Education

Impaired mucociliary clearance, decreased lung volumes, atelectasis, bed rest, diaphragmatic dysfunction, shallow breathing, and pain all contribute to the development of postoperative pulmonary complications. Various forms of chest physiotherapy including incentive spirometry, cough/deep breathing exercises, intermittent positive pressure breathing, and continuous positive airway pressure have been used with equal efficacy to minimize this risk [26]. In one study, 174 patients undergoing major abdominal surgery were randomized to either intervention with postoperative chest physiotherapy or control. Chest physiotherapy significantly reduced the incidence of both pneumonia, as well as all pulmonary complications (6% vs. 27%; $P<0.001$) [27].

The benefit of chest physiotherapy is even greater when patients participate in an intensive chest physiotherapy education session preoperatively. In a randomized controlled trial, 279 patients undergoing coronary artery bypass grafting were randomized to either “intensive muscle training” (IMT) or the control group. IMT program trained patients daily for a minimum of 2 weeks preoperatively in breathing exercises, forced exhalation techniques, and the use of inspiratory spirometry. The control group received instruction on deep breathing maneuvers, coughing and early ambulation on the day prior to surgery. Postoperative management of both groups was similar and consisted of incentive spirometry, chest physiotherapy, and mobilization. Compared with postoperative physiotherapy only, IMT further reduced the incidence of postoperative pulmonary complications (18% vs. 48%; $P=0.02$) and pneumonia (6.5% vs. 16.1%; $P=0.01$) by approximately 60% [28]. The reduction in pulmonary complications with preoperative physiotherapy education and training may relate to improved compliance and performance in the postoperative period [22].

Pulmonary Hypertension and Right Ventricular Function

Although primary pulmonary hypertension may in and of itself be a cause of ESLD, this is rare condition that has an incidence of only 1–2 per million [29, 30]. Much more commonly, pulmonary hypertension is the result of chronic hypoxemia and ESLD. The classification of pulmonary hypertension is summarized in Table 24.3. While estimates vary widely depending on disease severity and the method of measurement, the prevalence of pulmonary hypertension (mean PAP >25 mmHg) in advanced COPD, IPF, and CF ranges from 40 to 50% [31, 32]. As PAPs rise, evidence of cor pulmonale develops as increased strain causes the right ventricle to hypertrophy and become dysfunctional. In the United States, cor pulmonale accounts for 10–30% of all heart failure admissions, of which

TABLE 24.3. Classification of pulmonary hypertension.

1. Pulmonary arterial hypertension (PAH)
1.1. Idiopathic PAH
1.2. Heritable
1.2.1. Bone morphogenetic protein receptor type II gene abnormality
1.2.2. Activin receptor-like kinase 1 or endoglin gene abnormality (with or without hereditary hemorrhagic telangiectasia)
1.2.3. Unknown
1.3. Drug- and toxin-induced
1.4. Associated with
1.4.1. Connective tissue diseases
1.4.2. HIV infection
1.4.3. Portal hypertension
1.4.4. Congenital heart diseases
1.4.5. Schistosomiasis
1.4.6. Chronic hemolytic anemia
1.5 Persistent pulmonary hypertension of the newborn
2. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
3. Pulmonary hypertension owing to left heart disease
3.1. Systolic dysfunction
3.2. Diastolic dysfunction
3.3. Valvular disease
4. Pulmonary hypertension owing to lung diseases and/or hypoxia
4.1. Chronic obstructive pulmonary disease
4.2. Interstitial lung disease (ILD)
4.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
4.4. Sleep-disordered breathing
4.5. Alveolar hypoventilation disorders
4.6. Chronic exposure to high altitude
4.7. Developmental abnormalities
5. Chronic thromboembolic pulmonary hypertension (CTEPH)
6. Pulmonary hypertension with unclear multifactorial mechanisms
6.1. Hematologic disorders: myeloproliferative disorders, splenectomy
6.2. Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
6.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
6.4. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

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84% are secondary to COPD [31]. The risk of right ventricular ischemia is also increased. The right ventricle is normally perfused throughout the cardiac cycle. However, the increased right ventricular transmural and intracavitory pressures associated with pulmonary hypertension may restrict perfusion of the right coronary artery during systole, especially if PAPs approach systemic levels.

The impact of pulmonary hypertension on right ventricular dysfunction has several anesthetic implications. The cardiac goals are similar to other conditions in which cardiac output is relatively fixed. These are summarized in Table 24.4. Care should be taken to avoid physiologic states which will worsen pulmonary hypertension such as hypoxemia, hypercarbia, acidosis, and hypothermia. Conditions which impair right ventricular filling such as tachycardia and arrhythmias may not be well tolerated. Ideally, under anesthesia, right ventricular contractility and systemic vascular resistance (SVR) are maintained or increased while pulmonary vascular resistance (PVR) decreases. This would ensure forward flow and minimize the risk of right ventricular ischemia. In practice, these goals can be a challenge to achieve because anesthetics are commonly associated with either (1) a decrease in SVR and a variable effect on PVR (e.g., propofol, thiopental, inhalational agents), or (2) minimal effects on systemic and pulmonary vascular tone (e.g., benzodiazapines, opioids) [33]. Ketamine may be an interesting exception. Known for its sympathomimetic effects, ketamine increases cardiac contractility and SVR. However, its effect on PVR is controversial. Though concern is often raised over ketamine's potential to worsen pulmonary hypertension [34, 35], some animal in vitro and human clinical studies have suggested that it may decrease PVR [29, 33, 36]. Anecdotally, at the author's institution, ketamine is commonly and safely used to induce patients with severe pulmonary hypertension. Inotropes such as dobutamine and phosphodiesterase inhibitors (e.g., milronone) will improve right ventricular function while reducing PVR. However, they also cause systemic vascular tone to decrease.

TABLE 24.4. Anesthetic goals in pulmonary hypertension.

Optimize preload	Hypovolemia will further impair cardiac output Hypervolemia will precipitate right ventricular failure
Maintain a low-normal HR	Tachycardia will impair ventricular filling and cardiac output
Maintain RV contractility	Consider inotropes including epinephrine, norepinephrine, dobutamine, and phosphodiesterase inhibitors
Maintain or ↓ PVR	Avoid physiologic states that ↑ PVR (hypoxia, hypercarbia, acidosis, hypothermia) Consider using dobutamine, phosphodiesterase inhibitors, prostaglandins, or inhaled nitric oxide
Maintain or ↑ SVR	To maintain RV perfusion, SBP > PAP must be maintained Consider using vasopressors including norepinephrine, phenylephrine, and vasopressin

To maintain a systemic blood pressure (SBP) that is greater than the pulmonary, vasopressors such as phenylephrine or norepinephrine are commonly used. Of the two, norepinephrine is better suited in pulmonary hypertension because it maintains cardiac index and decreases the ratio of PAP to SBP [29, 33]. In contrast, phenylephrine causes the cardiac index to drop while the PAP:SBP ratio remains the same. Increasingly, vasopressin is also being used to maintain systemic pressures. On the basis of the limited data on humans, vasopressin appears to significantly increase SBP without affecting PAPs in patients with pulmonary hypertension (Fig. 24.2) [37–39]. In a rat model with preconstricted pulmonary vessels, vasopressin administration even led to pulmonary vasodilation. However, until better studies are available, vasopressin should be used cautiously because some human and animal studies have suggested that it causes pulmonary vasoconstriction [39]. In patients with severe pulmonary hypertension, selective pulmonary vasodilators including inhaled nitric oxide and inhaled prostaglandins should be considered. The effects of

medications on PVR are discussed in greater detail in Chap. 9. The extreme ends of patient lung volumes can cause compression of the extraalveolar and alveolar vessels, both of which contribute to an increased PVR (see Fig. 4.5 in Chap. 4). As a result, a ventilation strategy that avoids atelectasis as well as lung hyperinflation should be employed.

Nocturnal Hypoxemia

Sleep, even in normal individuals, is associated with physiologic changes in respiratory function. During all stages of sleep, the effectiveness of chemoreceptors and mechanoreceptors is reduced which leads to lower minute ventilation. This is particularly pronounced during rapid eye movement sleep. Decreased muscle contractility of the diaphragm as well as the accessory muscles further reduce the ventilatory response and contribute to the rapid shallow breathing observed during sleep.

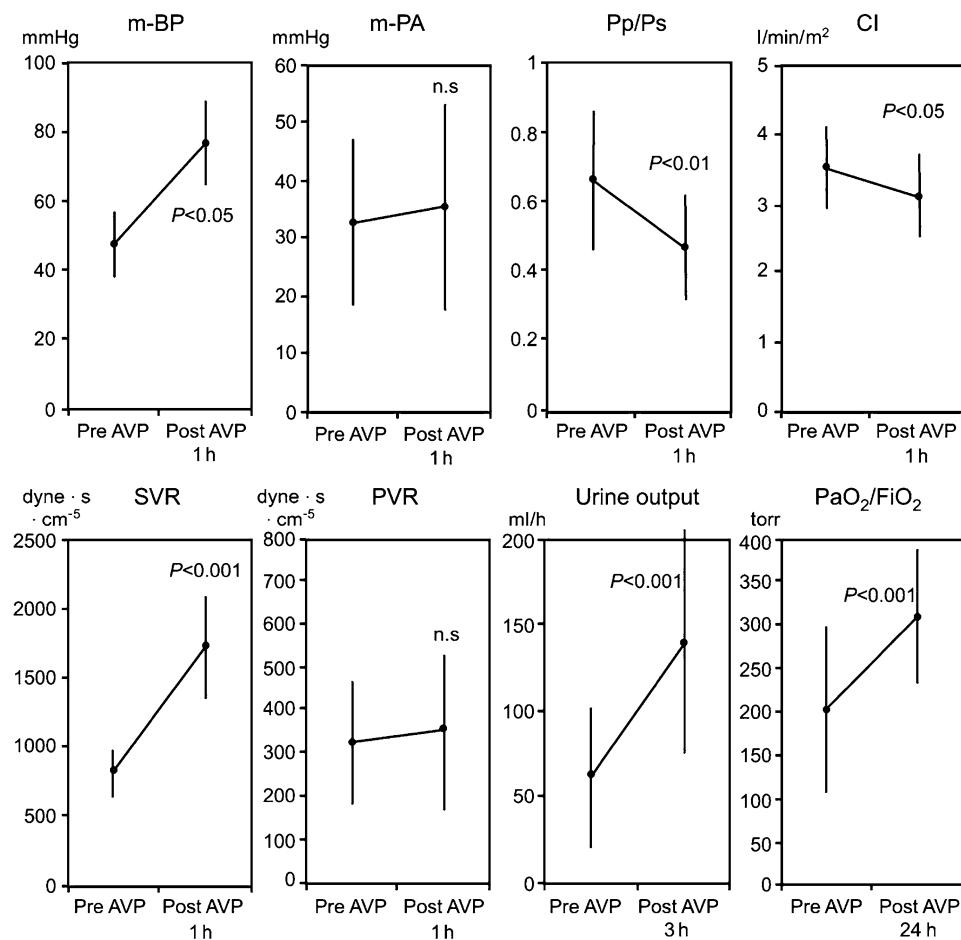


FIG. 24.2. Effect of arginine vasopressin (AVP) on mean systemic blood pressure (mSBP), mean pulmonary artery pressure (mPAP), pulmonary artery pressure/systemic blood pressure (Pp/Ps), cardiac index (CI), SVR, PVR, urine output, and $\text{PaO}_2/\text{FiO}_2$ (reprinted from Tayama et al. [37]. © 2007 with permission).

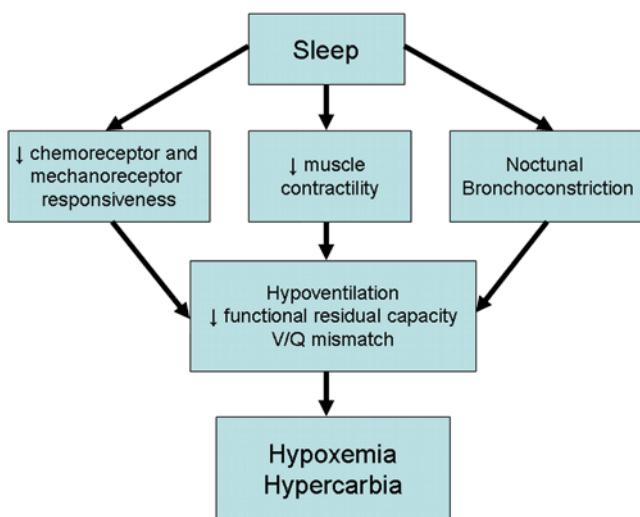


FIG. 24.3. The effects of sleep on breathing.

Normal fluctuations in the circadian rhythm also cause nocturnal bronchoconstriction. These changes, which are summarized in Fig. 24.3, result in a hypoventilation, decreased functional residual capacity (FRC), and increased ventilation-perfusion (V/Q) mismatch [40, 41]. In normal individuals this translates into an 8–10 mmHg drop in overnight P_aO_2 (arterial partial pressure of oxygen) levels [41].

The potential adverse cardiac (e.g., worsened pulmonary hypertension, RV failure, arrhythmia), neurologic, and hematologic (e.g., polycythemia) effects of nocturnal hypoxemia are particularly worrisome in patients with low daytime oxygen saturation. Though best studied in COPD and CF populations, other causes of ESLD including ILD and primary pulmonary hypertension have also been associated with higher rates of nocturnal hypoxemia [41–44]. Following surgery, a further fall in FRC and the use of opioid analgesia places these patients at high risk of severe hypoxemia during sleep. Although oxygen therapy is used successfully to minimize the incidence of desaturation overnight, there is no clear evidence that treatment of isolated nocturnal hypoxemia improves mortality [40, 45]. In some patients oxygen therapy may exacerbate the degree of hypercapnia.

Preoperative Assessment

The primary focus of the preoperative evaluation in patients with ESLD is the respiratory and cardiac systems. A history of patient symptoms, functional status, and activities of daily living, not to mention the physical examination, can be a valuable source of information. As discussed in Chap. 2, the patient's respiratory function needs to be assessed in terms of (1) respiratory mechanics, (2) lung parenchymal function, and (3) cardiopulmonary reserve. In this regard, pulmonary function testing is essential in determining the intraoperative management and postoperative disposition of patients with advanced

lung disease. While a detailed history is often sufficient for estimating cardio-pulmonary reserve, formal exercise testing or a 6-min walk test can be used to provide a quantitative assessment. A preinduction arterial blood gas should be drawn to establish the patient's baseline. The preoperative workup of patients with ESLD routinely includes a recent echocardiogram. However, while echocardiography is a common tool in the assessment of pulmonary hypertension and right ventricular dysfunction, it is limited by a low specificity of only 55% (sensitivity=85%) [31]. Echocardiography in patients with parenchymal lung disease may also result in suboptimal images. The presence of intracardiac lesions which may cause right to left shunting in the face of elevated right-sided pressures should be ruled out.

Intraoperative Monitoring

ESLD is frequently associated with a large arterial–end tidal CO_2 gradient. Placement of an arterial line facilitates intraoperative blood gas sampling to ensure adequate oxygenation and ventilation. In patients with pulmonary hypertension, continuous blood pressure monitoring is also reassuring. A central line is useful in monitoring and managing patients with moderate-to-severe pulmonary hypertension. Pulmonary artery catheters (PAC) may be of use in patients with PAPs which approach system pressures. However, the utility of PACs is controversial. From a large randomized trial, the use of PAC in ASA III and IV patients undergoing urgent or elective noncardiac surgery showed no effect on mortality or the incidence of postoperative pneumonia [46]. In addition, PAC use in patients with pulmonary hypertension is associated with a higher risk of pulmonary artery rupture.

Although nasogastric tubes are often routinely placed intraoperatively to facilitate postoperative gastric decompression, this practice is associated with an increased risk of pneumonia and atelectasis. In a meta-analysis of 24 studies, routine nasogastric tube use is associated with a statistically significant risk ratio of pulmonary complications (OR=1.4; 95% CI=1.08–1.93) [47]. As a result, routine postoperative nasogastric tube use should be avoided, especially in patients with poor baseline respiratory status.

General vs. Regional Anesthesia

Whether surgical outcomes are altered by the use of general or regional anesthesia has been a topic of debate for decades. Although the role regional anesthesia plays in reducing mortality, deep vein thrombosis, pulmonary embolism, cardiac ischemia, and blood loss remains controversial, current evidence suggests intraoperative neuraxial anesthesia followed by postoperative neuraxial analgesia reduces the incidence of postoperative pulmonary complications [48–53]. In a meta-analysis, neuraxial anesthesia significantly reduced the

risk of postoperative respiratory depression by 59% [48]. This may occur because general anesthesia decreases the number and activity of alveolar macrophages and inhibits mucociliary clearance, thereby increasing the risk of pulmonary infection [54]. General anesthesia, especially with inhalational agents, also causes atelectasis in dependent areas of lung, decreased FRC, and an increase in V/Q mismatching, all of which contribute to the development of hypoxia. Following thoracic or upper abdominal surgery, atelectasis and the reduction in FRC may persist for up to 2 weeks as a result of postoperative diaphragmatic dysfunction. Though the precise mechanism is unclear, this dysfunction appears to result from reflex inhibition of the phrenic nerve secondary to irritation of splanchnic afferents or visceral pain. There is evidence that postoperative epidural analgesia blocks the stimulus for the reflex inhibition and restores normal diaphragm function [54–56].

Park et al. randomized 1,021 ASA III or IV patients undergoing intraabdominal aortic, gastric, biliary, or colon operations to receive either (1) general anesthesia and systemic morphine for postoperative pain control, or (2) epidural anesthesia combined with a light general anesthesia and epidural morphine for postoperative pain. Overall, no difference in death or major complications were noted, although the epidural group did have a lower incidence of respiratory failure that approached significance ($P=0.06$). In a subgroup analysis of the 374 patients who underwent aortic surgery, epidural anesthesia did significantly reduce the incidence of myocardial infarction, stroke, and respiratory failure (14% vs. 28%; $P<0.01$) [49]. The subgroup analysis also showed a trend toward lower rates of pneumonia (51% vs. 71%; $P=0.06$). In another large trial by Rigg et al., 915 patients with one of nine high-risk comorbid states were randomized to receive either (1) general anesthesia and postoperative pain control with parenteral opioids or (2) combined epidural/general anesthesia and postoperative epidural analgesia. All patients had major abdominal surgery. Of the measured endpoints, the only difference was a reduction in respiratory failure in the epidural group (23.3% vs. 30.2%; $P=0.02$) [50].

The improved respiratory outcomes associated with regional anesthesia and analgesia are particularly important in patients with preexisting lung disease for whom the risk of developing a postoperative pulmonary complication is increased tenfold [57]. Moreover, patients with ESLD may be inherently more challenging to extubate following surgery and may require a prolonged ventilator wean. In recent years, the desire to avoid general anesthesia in severely compromised respiratory patients has led to several reports of neuraxial blockade being used as the sole anesthetic for intraabdominal procedures. van Zundert et al. [58] have successfully used a combined spinal-epidural placed at the T10 interspace to anesthetize a 47-year-old man with α -1-antitrypsin deficiency ($FEV_1/FVC=19\%$) for a laparoscopic cholecystectomy. Savas et al. [57] have reported using epidural anesthesia to facilitate awake surgery for sigmoidectomy, open cholecystectomy, incisional hernia repair, and laparoscopic inguinal hernia repair in patients with severe COPD. To date, we are only aware of one study that

specifically compares regional anesthesia vs. general anesthesia outcomes in an advanced lung disease population. In a small retrospective review of patients with COPD undergoing a mini-laparotomy for treatment of abdominal aortic aneurysms, Kalko et al. compared the outcomes of 10 patients who had surgery solely under regional anesthesia with 13 patients who received general anesthesia. The mean FEV_1 % predicted for both groups was 44%. No differences in morbidity or mortality were observed. However, the epidural group hospital length of stay was considerably shorter (6 ± 2.3 days vs. 10 ± 4.8 days; $P<0.031$) [59].

Ventilation and ESLD

In the last decade, the influence of ventilation strategy on ALI and acute respiratory distress syndrome (ARDS) has become clearer. The transition from high tidal volume (V_T) ventilation [$V_T=10\text{--}12$ mL/kg predicted body weight (PBW)] and zero end expiratory pressure (ZEEP) to low V_T lung ventilation ($V_T=6$ mL/kg PBW) with positive end expiratory pressure (PEEP) has improved survival, and become standard therapy in the management of patients with ALI and ARDS [60]. Whether patients without ALI or ARDS may also benefit from a low V_T ventilation strategy has been a subject of increasing interest and debate in both intensive care and anesthesia literature.

Tidal Volume

In one retrospective cohort study by Gajic et al., 332 patients without ALI/ARDS at the onset of mechanical ventilation and subsequently ventilated for greater than 48 h were assessed for the development of ALI/ARDS. Of these patients, 25% developed ALI. ALI, on average, appeared on the third day of ventilation. Following multivariate analysis, large tidal volume (OR = 1.3 for each milliliter above 6 mL/kg PBW) was determined to be a risk factor for the development of ALI [61].

Whether intraoperative ventilation strategy alters the risk of ALI is less clear [62, 63]. When 83 patients who developed ALI after major surgery were compared to 166 case-matched controls in a cohort observational study, tidal volume was not associated with increased risk of ALI. However, the difference in tidal volume between the two groups was small (8.7 mL/kg vs. 8.9 mL/kg PBW). Following multivariate analysis, the only ventilation parameter associated with reduced ALI was lower peak airway pressure (19 cm H₂O vs. 21 cm H₂O, $P=0.045$) [64]. In contrast, a retrospective study of 1,091 patients requiring lung cancer surgery, the use of lower tidal volumes (6.5 mL/kg vs. 9.2 mL/kg PBW during two-lung ventilation, 5.3 mL/kg vs. 7.1 mL/kg PBW during one-lung ventilation) was associated with a decreased incidence of ALI (0.9% vs. 3.7%, $P=0.032$), fewer admissions to ICU (2.5% vs. 9.4%, $P<0.001$) and shorter hospital length of stay (11.8 days vs. 14.5 days, $P<0.001$) [65]. Given the small incidence of postsurgical ALI, prospective studies examining the causal

relationship between ventilation strategies and lung injury have used inflammatory markers as a substitute indicator. In general, only studies in which patients were ventilated for longer than 5 h have shown a correlation between large tidal volume ventilation and increased inflammatory markers [62]. For example, Wolthuis et al. [66] randomly assigned patients undergoing major abdominal surgery lasting more than 5 h to either intraoperative ventilation with a tidal volume of 12 mL/kg plus ZEEP or to a tidal volume of 6 mL/kg plus 10 cm H₂O PEEP. When bronchoalveolar lavage fluid sampled after 5 h of ventilation was compared to baseline, the use of high tidal volumes resulted in a significantly greater rise in myeloperoxidase levels. However, intraoperative increases in inflammatory markers have, to date, not been linked to worse clinical outcomes. In a trial with 52 patients undergoing esophagectomy randomized to either (a) conventional ventilation with $V_T=9$ mL/Kg during both TLV and OLV and no PEEP, or (b) protective ventilation with $V_T=9$ mL/kg during TLV, $V_T=5$ mL/kg during OLV, and PEEP=5 cm H₂O throughout the procedure, plasma cytokines (IL-1, IL-6, IL-8) were found to be lower in the protective ventilation group. No differences in length of intensive care stay or postoperative morbidity were found [67].

With definitive evidence that low V_T ventilation improves outcome in patients with ALI/ARDS but only weak conflicting evidence that low tidal volumes intraoperatively may reduce the risk of developing ALI, the optimal intraoperative ventilation strategy is debatable. Many argue that traditional high V_T ventilation has been used for decades, and thus has a proven safety record. On the other hand, perhaps the high mortality associated with ALI, in spite of inconclusive evidence of causation, is sufficient reason to transition to low V_T ventilation. This may be particularly relevant to patients with ESLD, many of whom have an element of chronic pulmonary inflammation, and are the least likely to tolerate further injury. In a large study of 4,420 patients undergoing high-risk elective surgery, smoking and COPD were significant risk factors for the development of ALI ($P=0.005$ and $P=0.023$, respectively). In this study, ALI was associated with an in-hospital mortality of 17%, a threefold increase compared to patients without postoperative respiratory failure ($P=0.004$) [64]. It is worth noting that no studies comparing these two ventilation strategies have demonstrated a worse outcome by using low tidal volumes and PEEP. Recent reviews on this topic have recommended the use of low tidal volumes (6 mL/kg PBW), especially during OLV [62, 68–72].

Airway Pressures

High airway pressures have also been linked to ALI. In a retrospective analysis of 197 patients undergoing pneumonectomy by van der Werff et al. [73], patients ventilated with a peak airway pressure greater than 40 cm H₂O were significantly more likely to develop ARDS (RR=3.0, 95% CI=1.2–7.3). In Licker's study of 879 patients undergoing lung resection for cancer, 37 developed ALI. The ALI group had a mean peak

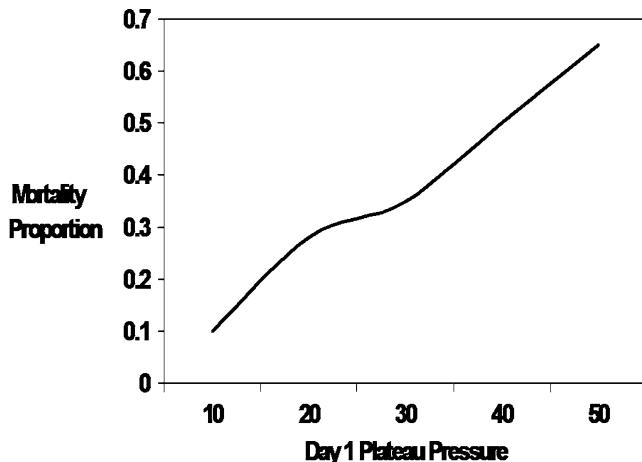


FIG. 24.4. Mortality and day 1 plateau pressure (P_{plat} ; cm H₂O) among patients enrolled in the Acute Respiratory Distress Syndrome Network (ARDSNet) study ($n=787$) (adapted from Hager et al. [75]).

inspiratory pressure of 29 cm H₂O compared to 18 cm H₂O in the non-ALI patients ($P=0.019$) [74]. From the Acute Respiratory Distress Syndrome Network (ARDSNet) trial, Hager et al. compared patient plateau pressures on day 1 of study enrollment with mortality. Their results, shown in Fig. 24.4, suggest that there is a relationship between increased plateau pressures and increased mortality, and that no plateau pressure can be considered “safe” [75].

While airway pressures may be minimized by using lower respiratory rates, ZEEP, and high inspiratory–expiratory (I:E) ratios, these ventilatory settings may be undesirable and inappropriate in certain settings. The mode of ventilation used will also impact peak airway pressures. Patients are commonly ventilated using volume control. In this mode, the ventilator delivers constant inspiratory flow (square wave pattern) which causes airway pressures to increase until the set tidal volume is achieved. Alternatively, pressure control ventilation (PCV) delivers maximal flow at the onset of inspiration until the set pressure is reached, after which the flow rapidly decreases (decelerating flow pattern) [70]. Compared to volume control ventilation (VCV), PCV results in lower peak airway pressures and more homogenous ventilation [70, 76]. However, with PCV the size of successive tidal volume breaths can be detrimentally affected by changes in lung compliance. In a study of ARDS patients, PCV resulted in peak airway pressures 5 cm H₂O less than VCV (26 ± 2 vs. 31 ± 2 cm H₂O; $P<0.001$) [77]. There is, however, no conclusive evidence that one mode of ventilation results in less risk of barotrauma, or improved gas exchange over the other [78].

Minimally Invasive Surgery

Key advantages of minimally invasive surgical procedures include reduced postoperative pain and an earlier return to baseline activities. For cholecystectomy and colorectal bowel resection, laparoscopic surgery results in less compromise

of FEV_1 and forced vital capacity (FVC), as well as a lower incidence of atelectasis on postoperative chest X-rays. In spite of these improved clinical measures, a significant difference in postoperative pulmonary complications has not been demonstrated [79, 80]. However, the anesthetic management of patients with ESLD undergoing laparoscopic surgery can be challenging. Laparoscopy causes a decrease in FRC which results in atelectasis and hypoxemia. Insufflation of CO_2 contributes to hypercarbia and respiratory acidosis. Although this is commonly controlled with increases in minute ventilation, this intervention may be of limited value in patients with gas exchange abnormalities. In the rare circumstance where patients with ESLD require awake laparoscopy under regional anesthesia, the additional CO_2 load may precipitate respiratory failure. The development of hypoxia, hypercarbia, and acidosis (all of which contribute to pulmonary vasoconstriction) can also significantly worsen the degree of pulmonary hypertension and right heart failure. As a result, ventilatory parameters and cardiac function must be carefully monitored, especially during abdominal CO_2 insufflation. If respiratory or cardiac decompensation occurs, abortion of the procedure or conversion to an open surgery should be considered.

Optimizing Emergence

Temperature monitoring should be used in patients with ESLD. Postoperative hypothermia and shivering significantly increase oxygen consumption and carbon dioxide production. Such an increase in ventilatory demand is poorly tolerated in ESLD, and may lead to respiratory failure. Intraoperative maintenance of normothermia with warming blankets and fluid warmers is extremely important.

While a variety of techniques and drugs may be used to safely induce and maintain anesthesia in patients with ESLD, agents with a short duration of action are preferred to minimize the risk of respiratory compromise at emergence. These patients are particularly sensitive to benzodiazepines and opioids, and thus, these drugs should be used sparingly. Drugs which bronchodilate and do not inhibit hypoxic pulmonary vasoconstriction (HPV) are also favored. In this respect, the newer inhalational agents, such as sevoflurane or desflurane, are well suited for most patients. However, as a result of diffusion abnormalities and ventilation-perfusion mismatch, the elimination of inhalational agents may be unpredictable in patients with ESLD and result in delayed awakening. In patients with baseline hypoxia and/or bullous disease, nitrous oxide should be avoided. Total intravenous anesthesia (TIVA) is a suitable alternative to inhalational anesthesia for maintenance. Intravenous anesthetics do not affect HPV and lead to a timely awakening once turned off. One TIVA combination that works well in this regard is propofol with remifentanil. Ketamine offers several distinct advantages including bronchodilation, preserved respiratory effort, and profound analgesic properties which may play a role in decreasing opioid

use postoperatively. However, ketamine is associated with a 5–30% risk of emergence delirium, and should be used cautiously [34].

Postoperative Analgesia

In patients with limited pulmonary reserve, effective postoperative pain management is essential. Splinting as a result of poorly controlled pain, especially from thoracic and abdominal surgery can contribute to increased pulmonary complications including respiratory failure. In patients without contraindications, the use of multimodal analgesic adjuvants including acetaminophen, nonsteroidal antiinflammatory drugs should be used. Although parenteral opioid use is effective in blunting pain, the amount needed following a thoracotomy or laparotomy may cause significant sedation and hypoventilation. Clearly, this is undesirable in patients with ESLD, especially those at risk of nocturnal hypoxemia. In comparison, a well functioning regional block (e.g., thoracic epidural, paravertebral block) consistently provides superior analgesia and improves respiratory mechanics [50, 81, 82]. In patients with severely compromised respiratory function, the use of regional analgesia in minimally invasive surgeries such as video-assisted thoracoscopic surgery or laparoscopy should be considered. For instance, epidural analgesia is standard for our patients with COPD undergoing video-assisted thoracoscopic LVRS. A complete discussion regarding postoperative analgesia is found in Chap. 46.

Chronic Obstructive Pulmonary Disease

With a prevalence of 4–9%, chronic obstructive pulmonary disease is the most common cause of ESLD [83]. The World Health Organization estimates that 210 million people worldwide suffer from the disease, and that it accounted for over three million deaths in 2005 [84]. COPD is a preventable disease characterized primarily by progressive expiratory airway obstruction that is not fully reversible. Significant extrapulmonary manifestations which contribute to disease severity include systemic inflammation, atherosclerosis, muscle weakness, and depression. Though most commonly associated with chronic bronchitis and emphysema, the COPD spectrum also includes asthma [83, 85, 86]. In fact, patients with active asthma are 10 times more likely to develop chronic bronchitis and 17 times more likely to develop emphysema [87]. Clinically, considerable overlap between these subtypes exists.

Diagnosis and Staging

The most commonly used spirometry criteria to diagnosis and stage COPD were developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). The diagnosis of COPD requires a FEV_1 to FVC ratio less than 0.7. The FEV_1

TABLE 24.5. The global initiative for chronic obstructive lung disease (GOLD) classification of COPD.

I	Mild	FEV ₁ /FVC < 70%
		FEV ₁ ≥ 80% predicted
II	Moderate	FEV ₁ /FVC < 70%
		50% ≤ FEV ₁ < 80% predicted
III	Severe	FEV ₁ /FVC < 70%
		30% ≤ FEV ₁ < 50% predicted
IV	Very severe	FEV ₁ /FVC < 70%
		FEV ₁ < 30% predicted

TABLE 24.6. Variables and point values used for the computation of the BODE Index.

Variable	Points on BODE Index			
	0	1	2	3
Body mass index	>21	≤21		
Airflow obstruction – FEV ₁ % predicted	≥65	50–64	36–49	≤35
Modified medical research council dyspnea scale	0–1	2	3	4
Exercise – Distance walked in 6 min (m)	≥350	250–349	150–249	≤149

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may then be used to stratify patients into one of four disease stages outlined in Table 24.5. Although FEV₁ % predicted can also be used to predict survival rates, the BODE index – a composite score that includes measures of body-mass index (B), airflow obstruction (O), dyspnea (D), and exercise capacity (E) – has been shown to be a better predictor of patient survival [88]. On the basis of patient investigations and clinical status, each variable is assigned a point value according to Table 24.6. Adding these points together gives the BODE index, which can range from 0 to 10. The Kaplan–Meier survival curves based on BODE index and FEV₁ are illustrated in Fig. 24.5. The improved accuracy of the BODE index over FEV₁ alone in predicting patient survival reflects the reality that COPD is more than a pulmonary disease, and that its outcome is closely related to systemic factors, including cardio-pulmonary reserve.

Etiology

The development of COPD is strongly associated with exposure to noxious gases and particles. One of the most important and certainly the most recognized causes of COPD is smoking, which accounts for 75–90% of all cases in western nations [84, 87]. Worldwide, however, the use of biomass fuel (wood, charcoal, vegetable matter, animal dung) for heating and cooking is a significant risk factor for COPD. In fact, compared to the number of cigarette smokers, nearly three times as many people are exposed to biomass smoke [87]. The WHO estimates that 22% of COPD is attributable to

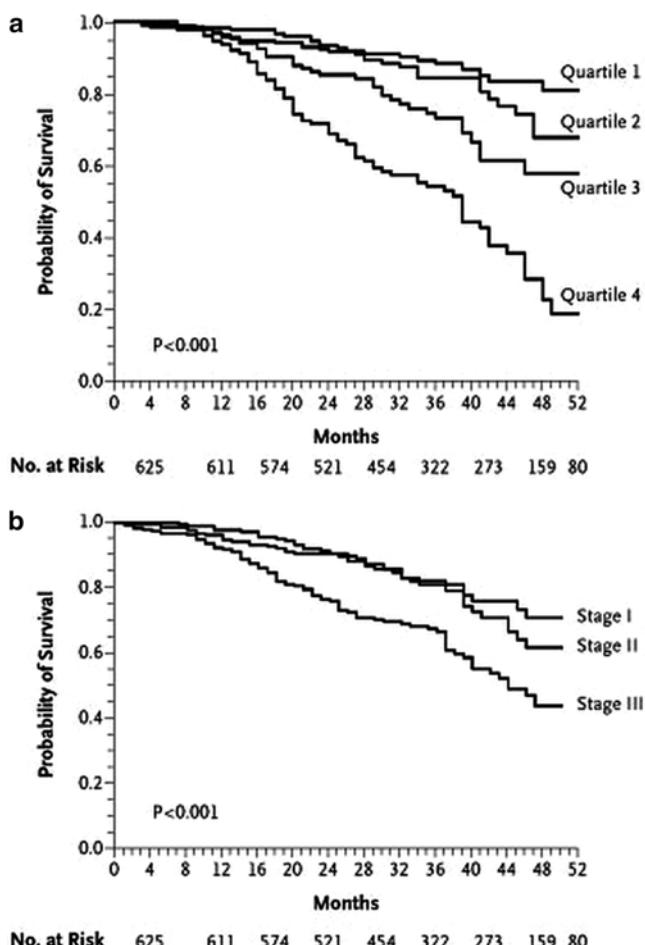
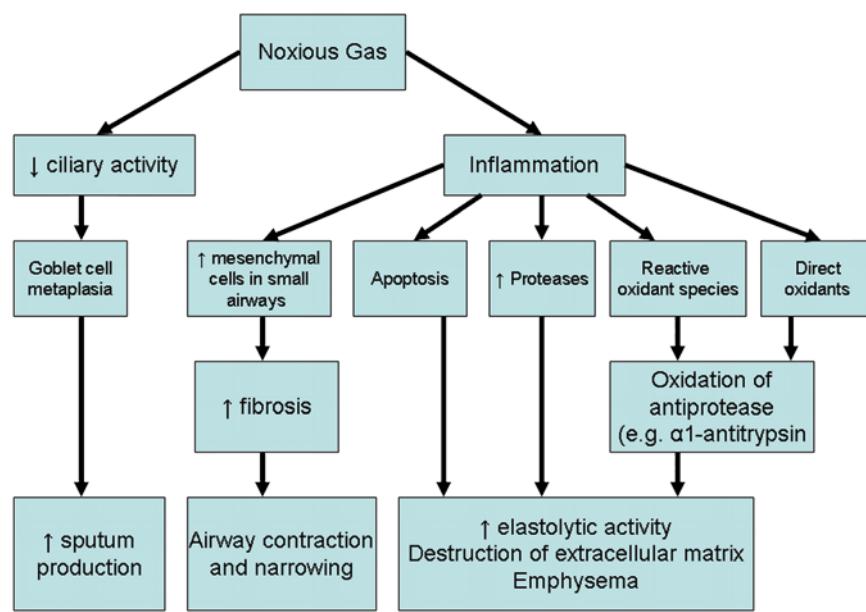


FIG. 24.5. Kaplan–Meier survival curves for the four quartiles of the BODE index (a) and the three stages of severity of chronic obstructive pulmonary disease as defined by the American Thoracic Society (b). In (a), quartile 1 is a score of 0–2, quartile 2 is a score of 3–4, quartile 3 a score of 5–6, and quartile 4 a score of 7–10. Survival differed significantly among the four groups ($P < 0.001$ by the log-rank test). In (b), stage I is defined by a forced expiratory volume in 1 s (FEV₁) that is more than 50% of the predicted value, stage II by an FEV₁ that is 36–50% of the predicted value, and stage III by an FEV₁ that is no more than 35% of the predicted value. Survival differed significantly among the three groups ($P < 0.001$ by the log-rank test) (reproduced with permission from Celli et al. [88]. © 2004 Massachusetts Medical Society. All Rights Reserved).

biomass smoke [84]. Other significant contributors include air pollution, occupational exposure, and a history of pulmonary tuberculosis [87]. The inhalation of noxious fumes triggers macrophages and neutrophils to release inflammatory mediators, cytokines, as well as proteases. Although proteases play an important role in preventing infection, they can also cause damage to lung tissue. The latter is normally prevented by the presence of antiproteases enzymes such as α -1 antitrypsin. However, chronic inflammation and inactivation of antiproteases by oxidants lead to an imbalance resulting in unopposed protease activity. Long-term exposure to this process

FIG. 24.6. Pathogenesis of chronic obstructive lung disease (COPD).



leads to fibrosis of the airway as well as destruction of alveoli [89]. The pathogenesis of COPD is summarized in Fig. 24.6.

COPD may also result from a number of genetic abnormalities, of which, α -1 antitrypsin deficiency is the most well known. Over 100 alleles have been identified for α -1 antitrypsin, the most common of which are the normal allele "M," and the abnormal alleles "S" and "Z." Although, only one normal allele ("M") is needed to produce the normal phenotype, heterozygote individuals ("MZ" or "MS") tend to produce 65% less α -1 antitrypsin than normal individuals ("MM") [84, 90]. The abnormal homozygote ("ZZ") which results in no α -1 antitrypsin production occurs with a prevalence between 1/1,575 and 1/5,097, and accounts for 2–3% of COPD [90]. While the disease onset varies, it is usually evident by the fourth or fifth decade, and even earlier in those who smoke [84]. In contrast to normal "MM" individuals who preferentially develop emphysematous changes in the apices, the distribution of emphysema in α -1 antitrypsin tends to be relatively homogeneous.

Causes of Expiratory Flow Obstruction

Expiratory flow limitation results from compression of the airways by intrathoracic pressure. In normal individuals this only occurs during forced expiration. The mechanism for this is shown in Fig. 24.7. Prior to inspiration and the initiation of flow, the airway pressure is zero throughout. With a resting intrapleural pressure of -5 cm water, a transmural pressure of 5 cm water maintains airway patency (Fig. 24.7a). With normal inspiration, both intrapleural and alveolar pressures decrease by 3 cm water, and flow begins (Fig. 24.7b). Although this pressure is transmitted into the airway, its magnitude progressively declines because of airway resistance. Assuming an airway pressure of

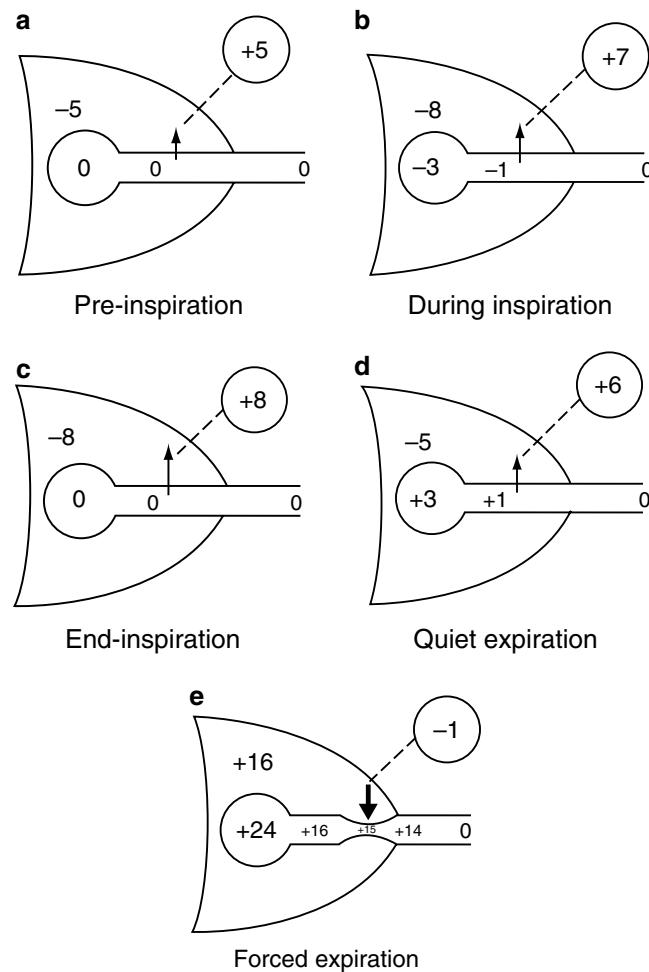


FIG. 24.7. The effect of intrapleural and alveolar pressures on airway patency (adapted from West [116]).

TABLE 24.7. Causes of flow limitation in COPD.

1. Loss of lung elastic recoil →
 - Reduced effective driving pressure
 - Reduced airway traction
2. Airway narrowing
3. Bronchospasm
4. Pulmonary secretions

–1 cm water during inspiration, then the airway is kept open by 7 cm water. At end-inspiration, the airway pressures return to zero as flow ceases (Fig. 24.7c). During exhalation an increase in both intrapleural and alveolar pressures occurs. As with inhalation, the transmitted pressure from the alveoli drops within the airway as a result of resistance. With quiet exhalation, the passive return of the lung and chest wall to their equilibrium positions generates a pressure of 3 cm water within the intrapleural space and alveoli (Fig. 24.7d). As a result, the pressure within the airway always exceeds the intrapleural pressure. In this example, pressures may increase up to 8 cm water without causing airway collapse. However, higher pressures associated with forced exhalation will lead to airway compression when the intraluminal pressure drops below the intrapleural pressure. This is called the equal-pressure point (EPP). Beyond this, further increases in expiratory effort (which will also increase intrapleural pressure) will only contribute to flow limitation and airway collapse. For example, if both intrapleural and alveolar pressures increase by 24 cm water during forced exhalation, then the EPP occurs at 16 cm water, below which airway collapse will occur (Fig. 24.7e). The effective driving pressure is therefore alveolar minus intrapleural pressure.

Factors that contribute to worsening flow limitation in patients with COPD are summarized in Table 24.7. Causes that may respond to intervention include active bronchospasm and airway obstruction by secretions. The loss of elastic recoil observed in emphysema results in less negative intrapleural pressures and reduces the outward traction normally exerted by lung parenchyma on the airway. This lowers both the transmural pressure which keeps the airway open as well as the effective driving pressure. In our COPD example shown in Fig. 24.8a, the intrapleural and the transmural pressure at end inspiration is –2 cm water, 6 cm water less negative than in a normal individual (see Fig. 24.7c). The propensity for airway collapse is accentuated by inflammatory and fibrotic changes which lead to contraction and narrowing of the small airways. As a result, even normal pressure increases of 3 cm water associated with quiet exhalation may result in flow limitation in patients with severe COPD (Fig. 24.8b).

Dynamic Hyperinflation

In COPD individuals, acute worsening of flow limitation may be precipitated by increased respiratory rates, physical activity, or COPD exacerbations. When flow limitation occurs, individuals with COPD are unable to exhale fully to FRC

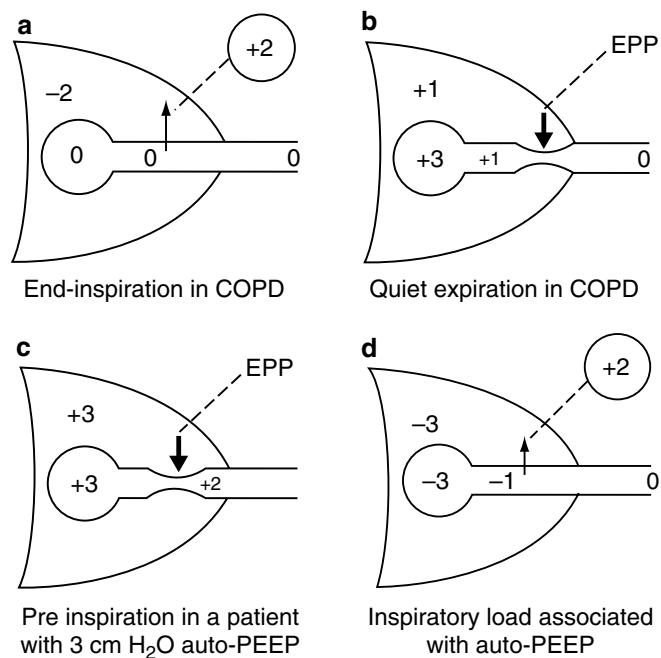


FIG. 24.8. The effect of intrapleural and alveolar pressures on airway patency in patients with COPD. EPP equal pressure point.

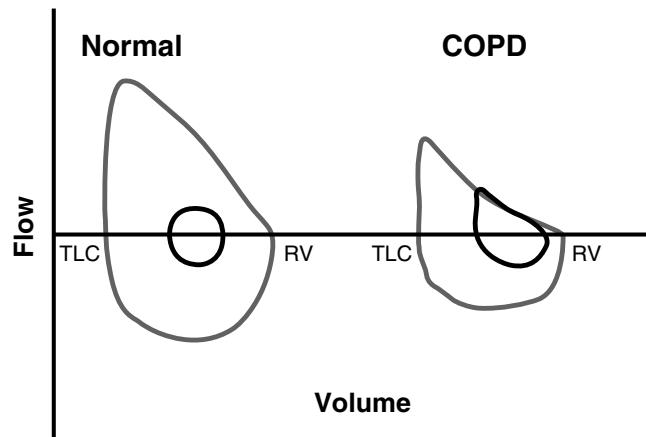


FIG. 24.9. Examples of flow–volume loops obtained in a healthy subject and a patient with COPD. The black lines represent the flow–volume loops at rest. The gray lines represent the maximal inspiratory and expiratory flow–volume loops (adapted from Pepin et al. [91]).

before their next inspiration. The positive pressure within the lung segments with air-trapping is referred to interchangeably as auto-PEEP or intrinsic PEEP (PEEP_i). With each subsequent inspiration, “breath-stacking” occurs and the alveoli become progressively more hyperinflated as auto-PEEP accumulates. Initially, auto-PEEP may improve respiratory mechanics and minimize the effect of flow limitation. Since patients with COPD generally expire along the maximum flow–volume loop envelop at rest, they have very limited ability to further increase expiratory flow (see Fig. 24.9) [91]. In this setting, low levels of auto-PEEP help

to temporarily improve ventilation by increasing the effective driving pressure, and thus expiratory flows.

However, as dynamic hyperinflation worsens the work of breathing increases dramatically. There are two reasons for this. First, for inspiratory flow to occur the alveolar pressure must be less than the atmospheric pressure. In normal individuals, this involves minimal effort. When auto-PEEP is present, an equivalent (and potentially large) amount of inspiratory pressure must be generated before airflow even begins. In essence, auto-PEEP is an additional inspiratory load [84, 92]. For example, if 3 cm water of auto-PEEP is present (Fig. 24.8c), then a typical inhalational effort of -3 cm water (see Fig. 24.7a, b) would only drop the alveolar pressure to atmospheric pressure. As a result, despite the pressure change, no inspiratory airflow would occur. In this example, to produce the -3 cm water pressure change required for a normal tidal volume breath (Fig. 24.7a, b), the COPD patient needs to generate an inspiratory pressure of -6 cm water (Fig. 24.8d). Second, dynamic increases in the end-expiratory lung volume results in each tidal volume breath shifting rightward of the flat portion of the volume-pressure compliance curve (see Fig. 24.10) [84, 91, 92]. This increases the work of breathing since a greater pressure must be generated in order to maintain a given tidal volume. Hyperinflation also leads to shortening of the inspiratory muscles, including the diaphragm, resulting in functional muscle weakness. Consequently, patients who develop dynamic hyperinflation experience significant dyspnea, respiratory distress, and muscle fatigue.

Hemodynamic instability is also common with high levels of dynamic hyperinflation. Increased intrathoracic pressure

associated with auto-PEEP reduces the pressure gradient for venous return into the thorax and also causes direct compression of the ventricles, both of which decrease preload and impair diastolic filling. High auto-PEEP will also increase PVR which may precipitate right ventricular dysfunction. In extreme cases, dynamic hyperinflation can cause cardiac arrest and subsequently impair resuscitation. The "Lazarus syndrome," in which patients recover from a cardiac arrest only after resuscitative efforts and positive pressure ventilation are stopped, has been attributed to resolving dynamic hyperinflation [93].

During anesthesia dynamic hyperinflation commonly presents with increasing airway pressures and severe hypotension shortly after induction when manual or mechanical ventilation is initiated. Other complications that may produce similar clinical findings include tension pneumothorax, anaphylaxis, and cardiac ischemia. When dynamic hyperinflation is suspected, the anesthetic circuit should be disconnected from the patient to permit full exhalation.

Intraoperatively, the build-up of intrinsic-PEEP can be difficult to assess. Ideally, the magnitude of auto-PEEP is measured directly at end-expiration. While this function is commonly found on intensive care ventilators, it is rarely available on anesthesia gas machines. However, the presence of intraoperative breath stacking can be indirectly assessed by capnography and spirometry loops. The capnograph tracing normally plateaus at the end of a fully exhaled breath, reflecting a constant alveolar concentration of CO_2 . In obstructive diseases, although the capnograph commonly up-slopes as a result of air from dead space diluting the exhaled CO_2 concentration, the capnograph will still plateau when exhalation is complete. If the next breath is initiated before the CO_2 plateaus, the presence of auto-PEEP should be suspected [86]. Similarly, the presence of air-trapping may be inferred from flow-volume loops when the expiratory flow does not drop to zero before the next breath (see Fig. 6.5 from Chap. 6).

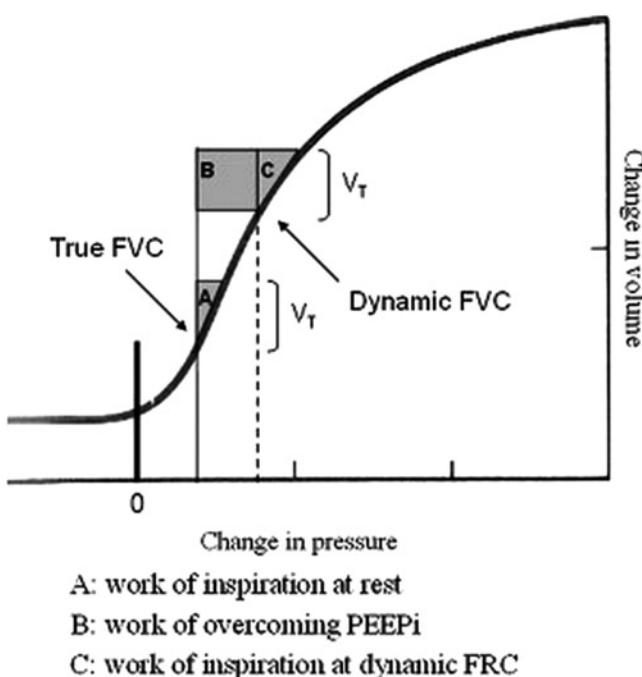


FIG. 24.10. Compliance curve of the lung (reprinted from Kemp et al. [84]. © 2009 with permission from Elsevier).

Respiratory Drive

The control of ventilation is primarily regulated by the arterial partial pressure of carbon dioxide (PaCO_2), with each 1 mmHg rise increasing minute ventilation by 2–5 L/min [94, 95]. However, this relationship is self-limiting. Within the central nervous system (CNS), severe hypercapnia and acidosis are associated with increased glutamine and gamma-aminobutyric acid (GABA), and decreased glutamate and aspartate levels. These changes result in a decreased level of consciousness, as well as reduced minute ventilation and inspiratory drive [94]. Typically, these CNS effects manifest when the PaCO_2 is greater than 60–70 mmHg. In patients with chronic hypercapnia that is compensated by an increase in bicarbonate, even higher PaCO_2 levels may be tolerated before respiratory depression occurs. In comparison with the linear minute ventilation response to PaCO_2 , decreases in the P_aO_2 lead to an exponential increase in minute ventilation only when levels fall below 60 mmHg.

Patients with stage III and stage IV COPD often have an elevated PaCO_2 at rest. Retention of carbon dioxide occurs because these patients are unable to maintain sufficient respiratory work to keep their PaCO_2 at normal levels. In these patients, clinicians have observed that oxygen administration can worsen the degree of hypercapnia. Traditionally, clinicians believed that patients with chronic hypercapnia had a blunted ventilatory response to increased PaCO_2 , and were dependent on hypoxic drive to breath. Supplemental oxygen would therefore inhibit hypoxic drive and decreased minute ventilation. While this explanation is valid, its contributing role to the overall increase in PaCO_2 is overstated. In one study of patients with COPD in acute respiratory failure, oxygen administration at 5 L/min only reduced the respiratory rate and the minute ventilation by 14% – an insufficient drop to account for the entire rise in PaCO_2 . Moreover, while ventilatory drive was reduced following oxygen supplementation, it remained three times greater than in normal individuals [96]. In another study, the rise in PaCO_2 that could be attributable to decreased minute ventilation was only 22%. In comparison, 48 and 30% of the PaCO_2 increase was attributed, respectively, to increases in dead-space ventilation and to reduced Haldane effect [97]. In patients with COPD, the degree of V/Q mismatching and dead-space ventilation is minimized by HPV which redirects blood away from poorly ventilated to well-ventilated areas. The use of supplemental oxygen decreases the beneficial effects of HPV, and as a result, CO_2 elimination is reduced. The Haldane effect describes the enhanced dissociation of CO_2 from red blood cells caused by the oxygenation of hemoglobin. Oxygenated hemoglobin has a much lower affinity for CO_2 than deoxygenated hemoglobin. As a result, deoxygenated hemoglobin facilitates the loading of CO_2 from peripheral tissue while the oxygenation of hemoglobin in the lungs leads to offloading. The magnitude of the Haldane effect is proportional to the difference between the mixed venous oxygen saturation and the arterial oxygen saturation. In other words, more CO_2 is released in the lungs when the mixed venous–arterial gradient is large. However, in patients with COPD this gradient is significantly reduced by the use of high inspired fractions of oxygen (FiO_2). The first reason relates to the oxyhemoglobin dissociation curve. When the FiO_2 is increased from 0.21 to 1.0, the increase in the mixed venous partial pressure of oxygen ($\text{P}_{\text{MV}}\text{O}_2$) is large (on the steep part of the O_2 dissociation curve) compared to the small change in $\text{P}_{\text{a}}\text{O}_2$ (on the flat part of the O_2 dissociation curve). Secondly, the inhibition of HPV associated with high FiO_2 causes blood to shunt through poorly ventilated lung segments that have a small $\text{P}_{\text{MV}}\text{O}_2$ - $\text{P}_{\text{a}}\text{O}_2$ gradient [98]. As a result, the Haldane effect and CO_2 elimination are diminished.

In spite of the potential increase in PaCO_2 associated with the administration of oxygen to patients with COPD, titrated oxygen therapy must be used to avoid hypoxia. With respect to patients in acute respiratory failure, the reduction in ventilatory drive associated with oxygen administration may actually be of benefit. A lower respiratory rate minimizes the

risk of dynamic hyperinflation, the work of breathing, and the potential for respiratory muscle fatigue. Patients requiring supplemental oxygen need to be closely monitored for signs of CNS depression and CO_2 narcosis. The $\text{P}_{\text{a}}\text{O}_2$ and the PaCO_2 should be routinely checked.

Bullae

Bullae are cystic air spaces in the lung parenchyma with a diameter greater than 1 cm. Most commonly, bullae develop as a result of worsening emphysematous disease. Bullae form when there is a loss of structural support tissue within a localized area. Preserved elastic recoil of the surrounding lung tissue places outward traction on bulla, causing it to enlarge. This results in the characteristic “inflated” look of bullae on chest X-rays and computed tomography scans. Although bullae appear to compress adjacent lung segments, direct measurements have conclusively shown that they are not under positive pressure [99]. Perhaps surprisingly, bullae do not contribute significantly to increased dead-space ventilation. In spite of unimpeded communication between the airways and bullae, very little airflow occurs. The lack of elastic recoil essentially prevents fully expanded bullae from emptying during exhalation, or from filling any further during inhalation. In addition, because bullae are relatively avascular, they do not participate in gas exchange. In patients with large bullae occupying more than a third of the hemithorax, a mixed restrictive–obstructive disease pattern may emerge as the volume available to the nonbulbous lung segments is reduced. The loss of structural integrity within bullae predisposes patients to serious complications including rupture, tension pneumothorax, and bronchopleural fistula. Although the risk of these adverse events is increased with positive pressure ventilation, it may be safely used so long as the airway pressures are kept low. Chest tube insertion and lung isolation may be required should these complications arise.

Ventilation Strategies in Patients with Obstructive Disease

Providing effective mechanical ventilation for patients with severe COPD can be challenging. Key goals, which at times conflict, include (1) avoiding dynamic hyperinflation, (2) avoiding barotrauma and volutrauma, and (3) maintaining adequate oxygenation and ventilation. As previously discussed, dynamic hyperinflation occurs when inadequate expiratory time leads to breath-stacking. This risk can be minimized by using low I:E ratios in the range of 1:3 to 1:5, as well as low respiratory rates. This may result in lower minute ventilation and cause hypercarbia and hypoxia, both of which worsen pulmonary hypertension and right ventricular strain. Higher tidal volumes may improve these gas exchange abnormalities, but in conjunction with low I:E ratios this may significantly increase airway pressures and expose patients to a higher risk of volutrauma or barotrauma.

In spontaneously breathing patients with obstructive lung disease, applying extrinsic PEEP that is equal to or less than the patient's auto-PEEP has been shown to reduce the work of breathing associated with air-trapping. In contrast, for mechanically ventilated patients, the use of extrinsic PEEP in patients with obstructive disease is controversial. While extrinsic PEEP worsens gas exchange and hemodynamics in some studies, others have demonstrated an improvement in expiratory air flow [86]. In one study of eight patients, Caramez et al. [100] examined the effect of increasing extrinsic-PEEP from 0 to 150% of intrinsic-PEEP using four different ventilatory settings. Using total-PEEP, FRC, and plateau pressure as markers of expiratory flow limitation, the pooled data reliably showed a biphasic response with either no change or a slight increase in flow limitation when extrinsic-PEEP was less than intrinsic-PEEP, followed by a sharp rise once intrinsic-PEEP was exceeded. However, when individual patient data were examined, three different responses to external PEEP were noted (see Fig. 24.11). In five patients, the use of external PEEP reduced air trapping and hyperinflation during at least one of the four ventilatory settings. Unfortunately, patient response to extrinsic PEEP was unpredictable and appeared to be independent of the disease, mechanics, or ventilation parameters. In another study by Jolliet et al. [101], the use of extrinsic PEEP at 80% of intrinsic PEEP significantly reduced the degree of intrinsic PEEP (7.8–4.4 cm H₂O; $P < 0.001$) as well as the volume of air trapping (216–120 mL; $P < 0.001$). In spite of these improvements, no change in hemodynamic parameters (mean arterial pressure and cardiac output) or gas exchange (P_aO₂ and PaCO₂) was noted. Clinical relevance aside, it is difficult to accurately measure the degree of intrinsic PEEP intraoperatively, and thus, select a level of extrinsic PEEP

that does not exceed it. Extrinsic PEEP that is greater than intrinsic PEEP will worsen expiratory flow and increase hyperinflation. Given the limited evidence of benefit, the inability to define a clear expiratory PEEP target, and the risk of exacerbating air-trapping, the use of extrinsic PEEP in mechanically ventilated patients with obstructive lung disease should be avoided.

Cystic Fibrosis

CF is an autosomal-recessive disorder that results in impaired transport of sodium, chloride, and water across epithelial tissue. This leads to abnormally viscous secretions which can cause obstruction of the respiratory tracts, pancreas, biliary system, intestines, and sweat glands. The organ systems that are affected are summarized in Table 24.8. Though most commonly associated with Caucasians (1:3,000), the disease also affects Hispanics (1:9,500), African Americans (1:15,300), and Asian Americans (1:32,100) [102]. With improved medical care over the last half century, the prognosis for patients with CF has improved dramatically from a mean survival age of 1 year in 1950 to a mean survival age of 37.4 years in 2007 (Fig. 24.12). The early mortality of CF is primarily the result of pulmonary complications, which include air-trapping, pneumothorax, massive hemoptysis, and respiratory failure [103, 104].

Pulmonary Manifestations

As with COPD, CF is characterized primarily by airflow obstruction, although varying degrees of restriction can also occur. Early in the disease, expiratory flow limitation is caused by the accumulation of thick dehydrated mucous in the respiratory tract that is difficult to expectorate. Inability to clear the thick purulent secretions enhances bacterial growth and as the disease advances, colonization of the airways with *Pseudomonas aeruginosa* and *Staphylococcus aureus* is considered normal. Infection with other bacteria, through less common, is often much more serious. For instance, *Burkholderia cepacia* is associated with rapid deterioration of pulmonary function, uncontrolled bronchopneumonia, and death. Although infection results in a massive influx of inflammatory cells into the airways, this immune response is ineffective once bacterial infection is established, and actually contributes to disease progression. Elastase released by neutrophils overwhelms the antiprotease mechanisms of the lung resulting in inflammatory destruction of airway supportive tissue, increased airway collapsibility during expiration, the development of bronchiectasis, and worsened airway obstruction. As a consequence of these airway changes ciliary function is impaired, further limiting the patient's ability to clear secretions. In some, reactive airway disease may also contribute to the airflow obstruction. As with other causes of obstructive lung disease, patients with CF are at increased

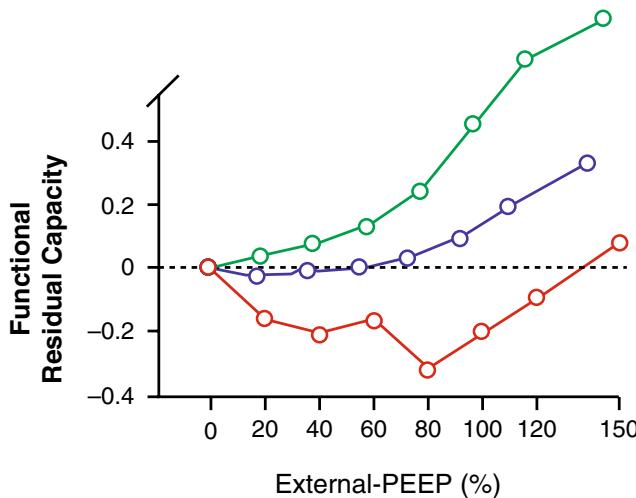


FIG. 24.11. The three potential responses in FRC when external-PEEP (represented as a percentage of PEEPi measured at zero external-PEEP) is applied. Blue is biphasic response; Green is classic overinflation response; and Red is paradoxical response.

TABLE 24.8. Clinical manifestations of cystic fibrosis.

Organ system	Clinical features	
Pulmonary	Impaired clearance of thick secretions Chronic inflammation → destruction of lung tissue → bronchiectasis Reactive airways Hemoptysis	Airway obstruction and air-trapping
Cardiac	Pulmonary hypertension and right ventricular failure	
Hepato-biliary	Obstruction of biliary duct → liver dysfunction Impaired synthesis of coagulation factors Bleeding from esophageal varices	
Pancreas	Hepato-splenomegaly → sequestration of platelets → thrombocytopenia Obstruction of pancreatic duct → pancreatitis Exocrine dysfunction → ↓ pancreatic enzymes → malabsorption of vitamins A, D, E, K → impaired synthesis of coagulation factors	
Gastrointestinal tract	Endocrine dysfunction → glucose intolerance	
Ears, nose, throat	Intestinal obstruction Large nasal polyps Sinusitis	

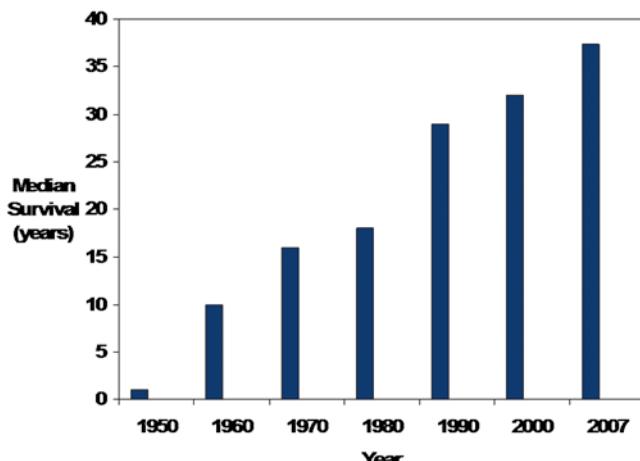


FIG. 24.12. Median age of survival for cystic fibrosis patients by year (adapted from Cystic Fibrosis Foundation Strategic Report 2009).

risk of dynamic hyperinflation and pneumothorax. Strategies that maintain low airway pressures and long expiratory times should be considered during mechanical ventilation. Chronic infection and inflammation also leads to increased airway vascularity through both bronchial artery hypertrophy and angiogenesis. The system of enlarged, dilated and tortuous vessels that develops is highly susceptible to trauma, and as a result, hemoptysis is common in patients with CF. Although most episodes of hemoptysis are self-resolving, some patients may require bronchial artery embolization or even surgical intervention [105]. In patients with hemoptysis requiring a general anesthetic, positive pressure ventilation may increase airway wall tension and precipitate massive hemoptysis. In one case report of 12 patients undergoing bronchial artery embolization who were managed with general anesthesia and intubation, three developed massive hemoptysis and died. In contrast, none of the eight patients managed with sedation developed massive hemoptysis [106].

Clearance of Pulmonary Secretions

Effective sputum elimination is a key goal in the long-term management of CF. A long-standing practice used to facilitate this is chest physiotherapy. Traditionally, this consisted of chest percussion with postural drainage. However, as more patients with CF survive into adulthood, there has been a shift toward forms of physiotherapy that can be performed independently. These alternatives range from simple breathing and coughing techniques to the use of medical devices of varying complexity [23]. Although chest physiotherapy is considered standard care, the number of quality trials examining its efficacy is limited. An analysis of five Cochrane systematic reviews concluded that there was insufficient data to evaluate the long-term benefits of chest physiotherapy [23]. Inhaled DNase I, a human recombinant enzyme that can decrease sputum viscosity by hydrolyzing extracellular DNA, has been shown to improve pulmonary function and reduce the incidence of pulmonary exacerbations. In a randomized controlled trial of 968 patients with CF, twice daily use of DNase I improved FEV₁ by approximately 6% ($P<0.01$) and reduced the risk of pulmonary exacerbations by 37% ($P<0.01$) [107]. Sputum viscosity can also be reduced by using inhaled hypertonic saline which osmotically draws water from the airway mucosa into the lumen. In a study of 164 patients, this therapy reduced the risk of pulmonary exacerbations by 56% ($P=0.02$) [108].

To optimize patients with CF for anesthesia, chest physiotherapy should be performed immediately prior to surgery. In patients who were prescribed inhaled DNase I and hypertonic saline, these should also be administered. Both during anesthesia and in the postoperative period, the viscosity of pulmonary secretions can be minimized by humidifying the inspired gases. Patient volume status needs to be carefully monitored to avoid both hypovolemia which may worsen secretion tenacity and hypervolemia which may trigger heart failure. Drugs which may either increase pulmonary secretions

(e.g., ketamine) or contribute to increased sputum viscosity (e.g., anticholinergics) are relatively contraindicated. Although supraglottic airways have been successfully used in patients with CF requiring general anesthesia, intubation with a large-sized endotracheal tube is usually preferred because it permits better control of ventilation and it facilitates endobronchial toileting with a suction catheter and/or fiberoptic bronchoscopy. When appropriate, the use of regional anesthesia and opioid-sparing adjuvant medications for management of post-operative pain is preferred. In addition to generalized respiratory depression, opioids may diminish the cough reflex, and thus sputum clearance.

Extrapulmonary Manifestations

Of the organ systems that are affected by CF, gastrointestinal dysfunction is particularly relevant to the anesthesiologist. Compared to normal individuals, gastro-esophageal reflux is 6–8 times more common in patients with CF, and may contribute to worsening respiratory symptoms [109]. Reflux symptoms should be treated aggressively, and precautions that minimize gastric acidity as well as the risk of aspiration should be considered during anesthesia (e.g., antacids, rapid sequence intubation). The buildup of thick secretions within the intestinal tract of patients with CF results in an increased risk of constipation and bowel obstruction. The use of narcotics may further exacerbate the potential for this complication. Though uncommon, patients with CF may develop a coagulopathy and have an increased risk of bleeding as a result of biliary duct obstruction. Generally, this only causes asymptomatic liver dysfunction. However, as the life expectancy of CF increases, the development of advanced liver disease and cirrhosis may produce complications such as bleeding from esophageal varices, impaired synthesis of coagulation factors, and thrombocytopenia secondary to hepato-splenomegaly. In addition, pancreatic exocrine insufficiency which results in malabsorption of protein, fat, as well as the fat-soluble vitamins is present in 85% of patients with CF [104]. Without supplementation, this causes a deficiency in vitamin K, an important precursor for the synthesis of coagulation factors X, IX, VII, and II. Pancreatic endocrine function may also be affected by CF. Approximately 75% of patients show evidence of glucose intolerance while 10% develop diabetes mellitus.

Pregnancy

The improved life expectancy associated with CF over the past few decades has led to a rise in the number of patients presenting for medical care while pregnant. In contrast to males with CF, of whom 95% are infertile, the fertility of young women with CF is almost unaffected [102, 110]. However, pregnancy is associated with a several physiologic changes that may stress the respiratory status of patients with CF. These include an increased oxygen consumption of 30–60%, an increased respiratory rate, decreased chest wall compliance, and decreased FRC. The patients with CF are also exposed to

an increased risk of respiratory infection because pregnancy results in a state of relative immunosuppression and maintenance chest physiotherapy becomes more difficult to perform. In spite of these concerns, recent studies suggest that long-term survival of pregnant patients with CF is similar (if not better) to that of never-pregnant patients with CF [111, 112].

The anesthetic management for this patient group follows the same principles already discussed for ESLD. In patients who require a cesarean section, the high risk of desaturation and difficult intubation associated with pregnancy combined with the respiratory impairment of CF strongly favors the use of regional anesthesia over general anesthesia. However, an inadvertent high block will also interfere with ventilation. Although spinal anesthesia is commonly used, the down side to a rapid onset dense block is that it can also cause significant vasodilation. In patients with pulmonary hypertension large decreases in systemic pressure may precipitate right ventricular ischemia. A titrated epidural results in less hemodynamic instability, greater control over block level, and provides superior postoperative pain management. Following delivery, uterotonic agents such as oxytocin and methylergonovine should be administered cautiously because they increase PVR. 15-Methyl prostaglandin F2- α (Hembate) not only increases PVR but can also result in significant bronchospasm, and should be avoided in patients with CF.

Interstitial Lung Disease

As with COPD and CF, inflammation plays an integral role in ILD. However, the inflammation associated with ILD results predominately in diffuse scarring and fibrosis of the alveolar walls and small airways, as opposed to tissue destruction. The factors which influence whether inflammation will precipitate one outcome vs. the other are unclear. About 35% of ILD is attributable to an identifiable cause such as exposure to inorganic dust, organic antigen, drugs, or radiation. In the remaining 65% of patients, even though the disease pattern may be given a specific name, the inciting agent resulting in ILD is unknown (Table 24.9).

Pulmonary Manifestations

As a consequence of inflammation and fibrosis of the alveolar walls, the elastic recoil of the lungs increase, they become less distensible, and lung volumes contract. Early in the disease, patients adapt to lower tidal volumes by increasing their respiratory rate. As the disease worsens, increased respiratory effort and energy are required to maintain sufficient tidal volumes to prevent alveolar hypoventilation. Uneven disease distribution throughout the lung can cause significant ventilation perfusion mismatch, and is the primary cause of hypoxemia in patients with ILD. Inflammation and fibrosis of the alveolar-capillary membrane also contribute to worsening oxygenation by reducing the surface area available for gas exchange and thus impairs diffusion.

TABLE 24.9. Common causes of ILD.

Known etiology	Unknown etiology
Inorganic dust	Idiopathic pulmonary fibrosis
Silicon dioxide → silicosis	Pulmonary fibrosis associated with connective tissue disease
Coal → coal worker's pneumoconiosis	Sarcoidosis
Asbestos → asbestosis	Eosinophilic granuloma
Beryllium → berylliosis	Goodpasture's syndrome
Organic antigen	Idiopathic pulmonary hemosiderosis
Thermophilic antinomycetes → farmer's lung	Wegener's granulomatosis
Bird proteins → bird breeder's lung	Chronic eosinophilic pneumonia
Drug induced	Bronchiolitis obliterans with organizing pneumonia
Chemotherapeutic	
Bleomycin	
Mitomycin	
Busulfan	
Cyclophosphamide	
Methotrexate	
Others	
Nitrofurantoin	
Gold	
Amiodarone	
Radiation induced	

Ventilation Strategy in Patients with Restrictive Lung Disease

Although a variety of techniques for general anesthesia have been used including airway management with an LMA and spontaneous ventilation, controlled ventilation through an endotracheal tube is the most reliable and safest approach to optimizing oxygenation and ventilation in patients with ILD when general anesthesia is required [113, 114]. The goals of mechanical ventilation in patients with ILD are to maintain adequate ventilation and oxygenation while minimizing the risks of barotrauma, volutrauma, and ALI. Potential strategies to minimize airway pressures include using high I:E ratios (e.g., 1:1 to 1:2), as well as low tidal volumes in conjunction with high respiratory rates. However, for each tidal volume breath, the latter strategy may result in a relative decrease in alveolar ventilation and exacerbate intraoperative hypercarbia and thus, the magnitude of pulmonary hypertension. Arterial blood gases should be closely monitored. In contrast to the obstructive lung diseases, PEEP can be safely used in ILD.

Clinical Case Discussion

A 70-year-old male presents with a small bowel obstruction and has been booked for a laparotomy. He has a history of severe COPD and has been prescribed home O₂ and a regime of daily puffers. Two months ago his FEV₁ and FEV₁/FVC were 35% predicted and 40%. He is a smoker with a 60 pack year history. Other medical issues include stable class 2 angina, hypertension, and dyslipidemia.

How Would You Optimize This Patient for Surgery?

- *Smoking cessation counseling.* Abstinence from cigarette use even for a few hours prior to surgery will result in lower carbon monoxide and nicotine levels. This may reduce the risk of intraoperative hypoxemia and cardiac stress. Postoperative compliance with smoking cessation improves wound healing and, in the long term, will decrease the rate at which FEV₁ declines.
- *Aggressive bronchodilation.* This patient requires maximal bronchodilator therapy. However, the use of β-agonists to achieve this goal must be balanced against the potential of precipitating ischemia in patients with coronary artery disease.
- *Steroid prophylaxis.* Coverage may be appropriate if the patient has been on long-term steroid therapy within the past year.
- *Physiotherapy education.* He will require aggressive chest physiotherapy postoperatively to minimize the risk of pulmonary complications. Early patient education and involvement will improve compliance and outcomes.

What Investigations Would You Like Prior to Induction?

- *Chest X-ray.* Pulmonary imaging will establish the degree of hyperinflation, and can help determine whether bullae are present. Given the increased risk of postoperative pulmonary complications in patients with COPD, a preoperative chest X-ray also provides a useful baseline comparison.
- *Arterial blood gas.* Establishing the degree of hypoxemia and whether the patient is a CO₂ retainer is essential to the intraoperative and postoperative management of patients with COPD.

How Would You Provide an Anesthetic for This Case?

- *Monitors.* In addition to the standard monitors (electrocardiogram, noninvasive blood pressure, pulse oximetry, capnography, agent detector), this patient will need an arterial line to monitor both respiratory status and hemodynamic stability. A central line may be useful to gauge fluid status as well as right ventricular function.
- *General vs. regional.* Although a sole regional technique may be considered, this may be poorly tolerated (for both surgeon and patient) when a large laparotomy is planned. When a general anesthetic is required, use in conjunction with epidural anesthesia and analgesia will minimize postoperative pulmonary complications.
- *Ventilation.* Given the high degree of expiratory airflow obstruction as well as the risk of lung injury, the ventilatory goals are: low airway pressures, low I:E ratios, and low respiratory rates. PEEP should be avoided.
- *Facilitate early extubation.* Postoperative respiratory depression must be avoided. Use short-acting agents. Fully reverse muscle relaxation. Consider TIVA over inhalational

- agents for maintenance of anesthesia. Patients must be aggressively warmed.
- **Postoperative care.** This patient requires optimal pain management. This is ideally achieved with an epidural analgesia and opioid-sparing adjuvant medications. He will also require observation in either a monitored unit or the intensive care unit.
- The patient suddenly becomes hypotensive 15 min into surgery. Specific to this patient's medical issues, what are the top differential diagnoses and what is the definitive management for each?
- **Tension pneumothorax.** Bilateral needle decompression followed by chest tube insertion.
 - **Dynamic hyperinflation.** Disconnect the breathing circuit to facilitate full exhalation.
 - **Cardiac ischemia.** This may be secondary to pulmonary hypertension or underlying CAD. Inotropes must be initiated to increase the blood pressure. Avoid medications and physiologic states that may worsen pulmonary hypertension and right ventricular failure. Consult cardiology for emergent angioplasty if coronary occlusion is suspected.
 - **Use of local anesthetics in the epidural.** Administer a vasoconstrictor in conjunction with a small fluid bolus.
- ## References
1. Casaburi R, Patessio A, Ioli F, et al. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. *Am Rev Respir Dis.* 1991;143(1):9–18.
 2. Meyer T, Faude O, Scharhag J, et al. Is lactic acidosis a cause of exercise induced hyperventilation at the respiratory compensation point? *Br J Sports Med.* 2004;38(5):622–5.
 3. Kesten S. Pulmonary rehabilitation and surgery for end-stage lung disease. *Clin Chest Med.* 1997;18(2):173–81.
 4. Donahoe M. Nutritional support in advanced lung disease. The pulmonary cachexia syndrome. *Clin Chest Med.* 1997;18(3):547–61.
 5. Casaburi R, ZuWallack R. Pulmonary rehabilitation for management of chronic obstructive pulmonary disease. *N Engl J Med.* 2009;360(13):1329–35.
 6. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. *Chest.* 2007;131(5 Suppl):4S–2.
 7. Cambach W, Wagenaar RC, Koelman TW, et al. The long-term effects of pulmonary rehabilitation in patients with asthma and chronic obstructive pulmonary disease: a research synthesis. *Arch Phys Med Rehabil.* 1999;80(1):103–11.
 8. Lacasse Y, Martin S, Lasserson TJ, et al. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane systematic review. *Eura Medicophys.* 2007;43(4):475–85.
 9. Ferreira G, Feuerstein M, Spiegler P. Results of an 8-week, outpatient pulmonary rehabilitation program on patients with and without chronic obstructive pulmonary disease. *J Cardiopulm Rehabil.* 2006;26(1):54–60.
 10. Kagaya H, Takahashi H, Sugawara K, et al. Effective home-based pulmonary rehabilitation in patients with restrictive lung diseases. *Tohoku J Exp Med.* 2009;218(3):215–9.
 11. Uchi M, Saji T, Harada T. Feasibility of cardiopulmonary rehabilitation in patients with idiopathic pulmonary arterial hypertension treated with intravenous prostacyclin infusion therapy. *J Cardiol.* 2005;46(5):183–93.
 12. Moorcroft AJ, Dodd ME, Morris J, et al. Individualised unsupervised exercise training in adults with cystic fibrosis: a 1 year randomised controlled trial. *Thorax.* 2004;59(12):1074–80.
 13. Nici L. Preoperative and postoperative pulmonary rehabilitation in lung cancer patients. *Thorac Surg Clin.* 2008;18(1):39–43.
 14. Cesario A, Ferri L, Galetta D, et al. Pre-operative pulmonary rehabilitation and surgery for lung cancer. *Lung Cancer.* 2007;57(1):118–9.
 15. Rajendran AJ, Pandurangi UM, Murali R, et al. Pre-operative short term pulmonary rehabilitation for patients of chronic obstructive pulmonary disease undergoing coronary artery bypass graft surgery. *Indian Heart J.* 1998;50(5):531–4.
 16. Bluman LG, Mosca L, Newman N, et al. Preoperative smoking habits and postoperative pulmonary complications. *Chest.* 1998;113:883–9.
 17. Fischer SP, Bader AM, Sweitzer BJ. Preoperative evaluation. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. *Miller's anesthesia.* 7th ed. Philadelphia, PA: Churchill Livingstone; 2009. p. 1022.
 18. Warner MA, Offord KP, Warner ME, et al. Role of preoperative cessation of smoking and other factors in postoperative pulmonary complications: a blinded prospective study of coronary artery bypass patients. *Mayo Clin Proc.* 1989;64(6):609–16.
 19. Nakagawa M, Tanaka H, Tsukuma H. Relationship between the duration of the preoperative smoke-free period and the incidence of postoperative pulmonary complications after pulmonary surgery. *Chest.* 2001;120:705–10.
 20. Barrera R, Weiji S, Amar D, et al. Smoking and timing of cessation. *Chest.* 2005;127:1977–83.
 21. Azodi OS, Lindstrom D, Adami J, et al. The efficacy of a smoking cessation programme in patients undergoing elective surgery – a randomized clinical trial. *Anaesthesia.* 2009;64:259–65.
 22. Warner DO. Preventing postoperative pulmonary complications. *Anesthesiology.* 2000;92:1467–72.
 23. Simon RH. Cystic fibrosis: overview of the treatment of lung disease. In: Mallory GB, editor. *UpToDate.* Waltham, MA: UpToDate; 2010.
 24. Barker AF. Treatment of bronchiectasis. In: Stoller JK, King TE, editors. *UpToDate.* Waltham, MA: UpToDate; 2010.
 25. Stroller JK. Management of acute exacerbations of chronic obstructive pulmonary disease. In: Barnes PJ, editor. *UpToDate.* Waltham, MA: UpToDate; 2010.
 26. Lawrence VA, Cornell JE, Smetana GW. Strategies to reduce postoperative pulmonary complication after noncardiothoracic surgery: systemic review for the American College of Physicians. *Ann Intern Med.* 2006;144:596–608.
 27. Olsen MF, Hahn I, Nordgren S, et al. Randomized controlled trial of prophylactic chest physiotherapy in major abdominal surgery. *Br J Surg.* 1997;84:1535–8.
 28. Hulzebos EH, Helders PJ, Favié NJ, et al. Preoperative intensive inspiratory muscle training to prevent postoperative pulmonary complications in high-risk patients undergoing CABG surgery: a randomized clinical trial. *JAMA.* 2006;296(15):1851–7.

29. Fischer LG, Van Aken H, Bürkle H. Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists. *Anesth Analg.* 2003;96(6):1603–16.
30. Blaise G, Langleben D, Hubert B. Pulmonary arterial hypertension: pathophysiology and anesthetic approach. *Anesthesiology.* 2003;99(6):1415–32.
31. Rovedder PM, Ziegler B, Pinotti AF, et al. Prevalence of pulmonary hypertension evaluated by Doppler echocardiography in a population of adolescent and adult patients with cystic fibrosis. *J Bras Pneumol.* 2008;34(2):83–90.
32. Han MK, McLaughlin VV, Criner GJ, et al. Pulmonary diseases and the heart. *Circulation.* 2007;116(25):2992–3005.
33. Subramaniam K, Yared JP. Management of pulmonary hypertension in the operating room. *Semin Cardiothorac Vasc Anesth.* 2007;11(2):119–36.
34. Stoelting RK, Hillier SC. Nonbarbiturate intravenous anesthetic drugs. In: Stoelting RK, Hillier SC, editors. *Pharmacology and physiology in anesthesia practice.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. p. 155–79.
35. Fox C, Kalarickal PL, Yarborough MJ, et al. Perioperative management including new pharmacological vistas for patients with pulmonary hypertension for noncardiac surgery. *Curr Opin Anaesthesiol.* 2008;21(4):467–72.
36. Friesen RH, Williams GD. Anesthetic management of children with pulmonary arterial hypertension. *Paediatr Anaesth.* 2008;18(3):208–16.
37. Tayama E, Ueda T, Shojima T, et al. Arginine vasopressin is an ideal drug after cardiac surgery for the management of low systemic vascular resistant hypotension concomitant with pulmonary hypertension. *Interact Cardiovasc Thorac Surg.* 2007;6(6):715–9.
38. Price LC, Forrest P, Sodhi V, et al. Use of vasopressin after Caesarean section in idiopathic pulmonary arterial hypertension. *Br J Anaesth.* 2007;99(4):552–5.
39. Smith AM, Elliot CM, Kiely DG, et al. The role of vasopressin in cardiorespiratory arrest and pulmonary hypertension. *QJM.* 2006;99(3):127–33.
40. Gay PC. Chronic obstructive pulmonary disease and sleep. *Respir Care.* 2004;49(1):39–51.
41. Bhullar S, Phillips B. Sleep in COPD patients. *COPD.* 2005;2(3):355–61.
42. Rafanan AL, Golish JA, Dinner DS, et al. Nocturnal hypoxemia is common in primary pulmonary hypertension. *Chest.* 2001;120(3):894–9.
43. Agarwal S, Richardson B, Krishnan V, et al. Interstitial lung disease and sleep: what is known? *Sleep Med.* 2009;10(9):947–51.
44. Milross MA, Piper AJ, Dobbin CJ, et al. Sleep disordered breathing in cystic fibrosis. *Sleep Med Rev.* 2004;8(4):295–308.
45. Gay PC. Treatment of sleep-disordered breathing in COPD. In: Basner RC, Sanders MH, Stoller JK, editors. *UpToDate.* Waltham, MA: UpToDate; 2010.
46. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med.* 2003;348(1):5–14.
47. Nelson R, Edwards S, Tse B. Prophylactic nasogastric decompression after abdominal surgery. *Cochrane Database Syst Rev.* 2007;(3):CD004929.
48. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ.* 2000;321(7275):1493.
49. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: a randomized, controlled Veterans Affairs cooperative study. *Ann Surg.* 2001;234(4):560–9.
50. Rigg JR, Jamrozik K, Myles PS, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet.* 2002;359(9314):1276–82.
51. Tziavrango E, Schug SA. Regional anaesthesia and perioperative outcome. *Curr Opin Anaesthesiol.* 2006;19(5):521–5.
52. Guler P, Nishimori M, Ballantyne JC. Regional anaesthesia versus general anaesthesia, morbidity and mortality. *Best Pract Res Clin Anaesthesiol.* 2006;20(2):249–63.
53. Breen P, Park KW. General anesthesia versus regional anesthesia. *Int Anesthesiol Clin.* 2002;40(1):61–71.
54. Rock P, Rich PB. Postoperative pulmonary complications. *Curr Opin Anaesthesiol.* 2003;16(2):123–31.
55. Kozian A, Schilling T, Hachenberg T. Non-analgesic effects of thoracic epidural anaesthesia. *Curr Opin Anaesthesiol.* 2005;18(1):29–34.
56. Drummond GB. Diaphragmatic dysfunction: an outmoded concept. *Br J Anaesth.* 1998;80(3):277–80.
57. Savas JF, Litwack R, Davis K, et al. Regional anesthesia as an alternative to general anesthesia for abdominal surgery in patients with severe pulmonary impairment. *Am J Surg.* 2004;188(5):603–5.
58. van Zundert AA, Stultiens G, Jakimowicz JJ, et al. Segmental spinal anaesthesia for cholecystectomy in a patient with severe lung disease. *Br J Anaesth.* 2006;96(4):464–6.
59. Kalko Y, Ugurlucan M, Basaran M, et al. Epidural anaesthesia and mini-laparotomy for the treatment of abdominal aortic aneurysms in patients with severe chronic obstructive pulmonary disease. *Acta Chir Belg.* 2007;107(3):307–12.
60. Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med.* 1998;338:347.
61. Gajic O, Dara SI, Mendez JL, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. *Crit Care Med.* 2004;32:1817.
62. Licker M, Fauconnet P, Villiger Y, et al. Acute lung injury and outcomes after thoracic surgery. *Curr Opin Anaesthesiol.* 2009;22(1):61–7.
63. Schultz MJ, Haitsma JJ, Slutsky AS, et al. What tidal volumes should be used in patients without acute lung injury? *Anesthesiology.* 2007;106(6):1226–31.
64. Fernández-Pérez ER, Sprung J, Afessa B, et al. Intraoperative ventilator settings and acute lung injury after elective surgery: a nested case control study. *Thorax.* 2009;64(2):121–7.
65. Licker M, Diaper J, Villiger Y, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. *Crit Care.* 2009;13(2):R41.
66. Wolthuis EK, Choi G, Dessing MC, et al. Mechanical ventilation with lower tidal volumes and positive end-expiratory pressure prevents pulmonary inflammation in patients without preexisting lung injury. *Anesthesiology.* 2008;108(1):46–54.
67. Michelet P, D'Journo XB, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology.* 2006;105:911.
68. Schultz MJ. Lung-protective mechanical ventilation with lower tidal volumes in patients not suffering from acute lung injury: a review of clinical studies. *Med Sci Monit.* 2008;14:RA22.

69. Lytle FT, Brown DR. Appropriate ventilatory settings for thoracic surgery: intraoperative and postoperative. *Semin Cardiothorac Vasc Anesth.* 2008;12:97.
70. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin.* 2008;26:241.
71. Grichnik KP, Shaw A. Update on one-lung ventilation: the use of continuous positive airway pressure ventilation and positive end-expiratory pressure ventilation – clinical application. *Curr Opin Anaesthesiol.* 2009;22:23.
72. Gothard J. Lung injury after thoracic surgery and one-lung ventilation. *Curr Opin Anaesthesiol.* 2006;19:5.
73. van der Werff YD, van der Houwen HK, Heijmans PJ, et al. Post-pneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest.* 1997;111:1278.
74. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97:1558.
75. Hager DN, Krishnan JA, Hayden DL, et al. Tidal volume reduction in patients with acute lung injury when plateau pressures are not high. *Am J Respir Crit Care Med.* 2005;172(10):1241–5.
76. Bozyk P, Hyzy RC. Modes of mechanical ventilation. In: Parsons PE, editor. UpToDate. Waltham, MA: UpToDate; 2010.
77. Prella M, Feihl F, Domenighetti G. Effects of short-term pressure-controlled ventilation on gas exchange, airway pressures, and gas distribution in patients with acute lung injury/ARDS: comparison with volume-controlled ventilation. *Chest.* 2002;122(4):1382–8.
78. Nichols D, Haranath S. Pressure control ventilation. *Crit Care Clin.* 2007;23(2):183–99.
79. Lawrence VA, Cornell JE, Smetana GW, et al. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med.* 2006;144(8):596–608.
80. Abraham NS, Young JM, Solomon MJ. Meta-analysis of short-term outcomes after laparoscopic resection for colorectal cancer. *Br J Surg.* 2004;91(9):1111–24.
81. Conacher ID, Slinger PD. Pain management. In: Kaplan JA, Slinger PD, editors. *Thoracic anaesthesia.* 3rd ed. Philadelphia, PA: Churchill Livingstone; 2003. p. 436–62.
82. Groeben H. Epidural anesthesia and pulmonary function. *J Anesth.* 2006;20:290–9.
83. Yamakage M, Iwasaki S, Namiki A. Guideline-oriented perioperative management of patients with bronchial asthma and chronic obstructive pulmonary disease. *J Anesth.* 2008;22(4):412–28.
84. Kemp SV, Polkey MI, Shah PL. The epidemiology, etiology, clinical features, and natural history of emphysema. *Thorac Surg Clin.* 2009;19(2):149–58.
85. Rennard SI. Chronic obstructive pulmonary disease: definition, clinical manifestations, diagnosis, and staging. In: Stoller JK, editor. UpToDate. Waltham, MA: UpToDate; 2010.
86. Erdich T, Sadovnikoff N. Anesthesia for patients with severe chronic obstructive pulmonary disease. *Curr Opin Anaesthesiol.* 2010;23(1):18–24.
87. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet.* 2009;374(9691):733–43.
88. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med.* 2004;350(10):1005–12.
89. Spurzem JR, Rennard SI. Pathogenesis of COPD. *Semin Respir Crit Care Med.* 2005;26(2):142–53.
90. Stoller J. Clinical manifestations, diagnosis, and natural history of alpha-1 antitrypsin deficiency. In: Barnes PJ, editor. UpToDate. Waltham, MA: UpToDate; 2010.
91. Pepin V, Saey D, Laviolette L, Maltais F. Exercise capacity in chronic obstructive pulmonary disease: mechanisms of limitation. *COPD.* 2007;4(3):195–204.
92. O'Donnell DE, Parker CM. COPD exacerbations-3: pathophysiology. *Thorax.* 2006;61(4):354–61.
93. Ben-David B, Stonebreaker VC, Hershman R. Survival after failed intraoperative resuscitation: a case of “Lazarus syndrome”. *Anesth Analg.* 2001;92:690–2.
94. Feller-Kopman DJ, Schwartzstein RM. Use of oxygen in patients with hypercapnia. In: Stoller JK, editor. UpToDate. Waltham, MA: UpToDate; 2010.
95. West JB. Control of ventilation. In: West JB, editor. *Respiratory physiology.* 5th ed. Baltimore, MD: Williams & Wilkins; 1990. p. 117–32.
96. Aubier M, Murciano D, Fournier M, et al. Central respiratory drive in acute respiratory failure of patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis.* 1980;122(2):191–9.
97. Aubier M, Murciano D, Milic-Emili J, et al. Effects of the administration of O₂ on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. *Am Rev Respir Dis.* 1980;122(5):747–54.
98. Hanson III CW, Marshall BE, Frasch HF, et al. Causes of hypercarbia with oxygen therapy in patients with chronic obstructive pulmonary disease. *Crit Care Med.* 1996;24(1):23–8.
99. Morgan MD, Edwards CW, Morris J, et al. Origin and behaviour of emphysematous bullae. *Thorax.* 1989;44(7):533–8.
100. Caramez MP, Borges JB, Tucci MR, et al. Paradoxical responses to positive end-expiratory pressure in patients with airway obstruction during controlled ventilation. *Crit Care Med.* 2005;33(7):1519–28.
101. Jolliet P, Watremez C, Roeseler J, et al. Comparative effects of helium-oxygen and external positive end-expiratory pressure on respiratory mechanics, gas exchange, and ventilation-perfusion relationships in mechanically ventilated patients with chronic obstructive pulmonary disease. *Intensive Care Med.* 2003;29(9):1442–50.
102. Karlet MC. An update on cystic fibrosis and implications for anaesthesia. *AANA J.* 2000;68(2):141–8.
103. Howell PR, Kent N, Douglas MJ. Anaesthesia for the parturient with cystic fibrosis. *Int J Obstet Anesth.* 1993;2(3):152–8.
104. Walsh TS, Young CH. Anaesthesia and cystic fibrosis. *Anaesthesia.* 1995;50(7):614–22.
105. Stenbit A, Flume PA. Pulmonary complications in adult patients with cystic fibrosis. *Am J Med Sci.* 2008;335(1):55–9.
106. McDougall RJ, Sherrington CA. Fatal pulmonary haemorrhage during anaesthesia for bronchial artery embolization in cystic fibrosis. *Paediatr Anaesth.* 1999;9(4):345–8.
107. Fuchs HJ, Borowitz DS, Christiansen DH, et al. Effect of aerosolized recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. The Pulmozyme Study Group. *N Engl J Med.* 1994;331(10):637–42.
108. Elkins MR, Robinson M, Rose BR, et al. A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. *N Engl J Med.* 2006;354(3):229–40.
109. Katkin JP, Schultz K. Cystic fibrosis: overview of gastrointestinal disease. In: Klish WJ, Mallory GB, editors. UpToDate. Waltham, MA: UpToDate; 2010.
110. Tonelli MR, Aitken ML. Pregnancy in cystic fibrosis. *Curr Opin Pulm Med.* 2007;13(6):537–40.

111. Bose D, Yentis SM, Fauvel NJ. Caesarean section in a parturient with respiratory failure caused by cystic fibrosis. *Anaesthesia*. 1997;52(6):578-82.
112. Goss CH, Rubenfeld GD, Otto K, Aitken ML. The effect of pregnancy on survival in women with cystic fibrosis. *Chest*. 2003;124(4):1460-8.
113. Carron M, Marchet A, Ori C. Supreme laryngeal mask airway for laparoscopic cholecystectomy in patient with severe pulmonary fibrosis. *Br J Anaesth*. 2009;103(5):778-9.
114. Schure AY, Holzman RS. Anesthesia in a child with severe restrictive pulmonary dysfunction caused by chronic graft-versus-host disease. *J Clin Anesth*. 2000;12(6):482-6.
115. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classifications of pulmonary hypertension. *J Am Coll Cardiol*. 2009;54:S43.
116. West JB. Mechanics of breathing. In: West JB, editor. *Respiratory physiology*. 5th ed. Baltimore, MD: Williams & Wilkins; 1990. p. 117-32.

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Key Points

- As the population ages, increasing numbers of elderly patients are present for thoracic surgery.
- Physiologic changes that occur with advanced age result in a decline of maximal reserves, affecting the patient's ability to cope with the stress of surgery. Increased age is also associated with increased comorbidities.
- Elderly patients with cancer may still stand to benefit from surgery, since survival rates for lung and esophageal cancer are very low without surgical resection.
- Perioperative morbidity and mortality is more closely associated with preoperative health status and tumor stage than chronological age.
- Minimally invasive surgical techniques such as video-assisted thoracoscopic surgery (VATS) have been shown to be an effective approach for surgical resection of cancer.
- Because better postoperative pulmonary function, less postoperative pain, and fewer complications were shown for patients who underwent VATS compared to those who underwent thoracotomy for lobectomy, VATS may be a good choice for patients of advanced age due to their decreased physiologic reserves.

- Careful preoperative assessment and postoperative care are essential in this surgical population due to their diminished ability to handle the stress of surgery.

Introduction

Demographic projections indicate that by the year 2030 the number of United States citizens over the age of 65 will exceed 70 million with those over 80 years of age comprising about 5% of the total population [1]. Currently, centenarians are the fastest growing segment of the population, a phenomenon that underscores the public health issues presented by an aging citizenry [1–3].

Lung cancer, the major reason for most thoracic surgery and the primary focus of this chapter, is particularly prominent in the elderly. As such, anesthesiologists are increasingly presented with the task of caring for patients exhibiting not only the normal physiological changes associated with aging but also a wide range of age-related comorbidities. In that fundamental aspects of preoperative evaluation, anesthetic pharmacology, and postoperative management are reviewed in other sections, this chapter shall primarily focus upon the

cardiopulmonary and hepato-renal ramifications of aging, the impact of aging on the thoracic surgical population, the risk-benefit relationship of thoracic surgery for the treatment of cancer in the elderly, and the emerging role of minimally invasive surgical techniques.

Physiology of Aging

Appreciation of the fact that the elderly population is expanding in both size and range underscores the importance of understanding the physiology of senescence. Ultimately, peri-operative management of the elderly thoracic surgical candidate is often more complex than that of younger patients due to both the physiologic changes associated with advanced age and the increased incidence of comorbidities, particularly cardiovascular pathology and chronic obstructive pulmonary disease (COPD). In general, as people age, their maximal physiologic reserves decline, potentially limiting their ability to respond adequately to the stress presented by a major operation or acute illness. Functionally, elderly patients may experience symptoms indicative of pathology that are blunted or diminished in intensity, are atypical, or may be misdiagnosed as simply due to “old age” [4].

Cardiovascular

A variety of molecular and structural changes occur within the aorta, myocardium, and cardiac conduction system that are, at least in part, interrelated and adaptive within certain limits [5–7] (Table 25.1). For example, aging is associated with an increase in left ventricular (LV) afterload due to an increase in the stiffness of large elastic arteries and the resultant increased

TABLE 25.1. Cardiovascular changes with aging.

Cardiac	Left ventricular hypertrophy-increased mass and decreased compliance Increased fatty infiltration, fibrosis, amyloid, and altered collagen cross-linking Increased risk of conduction defects Increased stroke work Slower myocardial relaxation (decreased lusitropy)
Vascular	Increased characteristic impedance and peripheral vascular resistance Increased incidence of coronary artery disease, plaques, calcified lesions, and fixed stenoses Decreased arterial elasticity with increased pulse pressure Aortic dilation with decreased compliance and higher wall tension
Reflex regulation	Decreased baroreceptor sensitivity Diminished myocardial chronotropic and inotropic response to catecholamines Decreased maximal cardiac output and heart rate Decreased autonomic control of peripheral vascular resistance

Adapted from Castillo and Heerd [7]

pulse wave velocity. Advanced age is also associated with increased LV mass secondary to myocyte hypertrophy, myocardial fibrosis, and valvular sclerosis and calcification. Vascular stiffness occurs secondary to the breakdown of elastin and collagen. Accompanying these structural changes are subcellular alterations in myocyte calcium cycling that allow the ventricle to maintain tension against the increased afterload for a longer period of time [6]. However, while this adaptation can be beneficial under some conditions, it can be maladaptive in others, such as tachycardia, when delayed relaxation can impede chamber filling. Superimposed on the direct changes that occur in the heart and circulation is a dampening of homeostatic reflexes that can serve to amplify the functional impact of an age-related decline in cardiovascular reserve [6].

Pulmonary

In general, the aging process is associated with alterations in the lung parenchyma, the chest wall “bellows” function, and central regulation of respiration (Table 25.2). Not surprisingly, respiratory complications are a major cause of morbidity and

TABLE 25.2. Respiratory changes with aging.

Structural	Decreased number of alveoli Decreased number of lung capillaries Decreased elastic recoil, causing easier collapse of peripheral airways Decreased airway size Decreased alveolar-capillary surface area Decreased negative intrapleural pressure Weakening of respiratory muscles Stiffer chest wall due to fibrosis and calcification
Secretory and immune	Less efficient mucociliary transport Less sensitive protective airway reflexes Diminished delayed-type hypersensitivity response to foreign antigens Increased response to autologous antigens Decreased polymorphonuclear leukocyte function
Central regulation	Blunted ventilatory response to hypoxia Blunted ventilatory response to hypercarbia
Functional manifestations	Increased periodic breathing during sleep Increased functional residual capacity (FRC) Increased air trapping Decreased forced expiratory volume exhaled in 1 s (FEV1) Decreased forced vital capacity (FVC) Decreased diffusing capacity Decreased venous blood oxygenation Increased closing capacity Decreased maximal voluntary ventilation (MVV) Increased work of breathing Widened alveolar-arterial gradient for oxygen Increased dead-space fraction Increased ventilation-perfusion mismatch Increased propensity for infection Decreased resting PaO_2

Adapted from Castillo and Heerd [7]

mortality after thoracic surgery. However, risk generalizations regarding the elderly population are difficult due to wide differences in functional status, largely reflecting the overlay of pathologic changes (i.e., COPD) on basic age-related changes. Thus, functional status clearly determines perioperative risk more than age alone [4]. Nonetheless, all elderly patients – regardless of functional status – will exhibit structural, secretory, and regulatory changes that can affect both ventilation and respiration [7, 8]. The integration of these changes with perioperative events can impact even short-term outcomes. For example, if an 80-year-old begins to shiver in response to hypothermia following a thoracotomy, the ability to compensate for increased carbon dioxide production is dampened intrinsically by reduced responsiveness of the central nervous system to drive ventilation coupled with impaired chest wall mechanics and alveolar gas exchange. Superimposed on these effects are the extrinsic effects of opiates to further depress central responsiveness and the added mechanical deficit imposed by thoracotomy. Ultimately, the patient is placed at increased risk of developing significant hypercarbia.

Hepato-Renal

Aging produces progressive changes in the liver and kidneys (Table 25.3) that can have a profound effect on drug metabolism and clearance [5]. By the age of 80 years, liver size decreases by as much as 40% and renal tissue mass has decreased by 30% [9]. At the same time, age-related changes in the perfusion patterns of organs in the body result in decreased blood flow to the liver and kidneys [9]. Ultimately, the decrease in size and perfusion of the liver can affect the plasma clearance of opiates, barbiturates, benzodiazepines, propofol, etomidate, most nondepolarizing relaxants, and other drugs metabolized by the liver [5]. Tissue atrophy and reduced renal blood flow result in decreased glomerular filtration rate, creatinine clearance, renal functional reserve, responsiveness to antidiuretic hormone, and increased susceptibility to renal ischemia and acute renal failure. These age-related changes result in the prolongation of the elimination half-time of drugs and metabolites requiring renal clearance. As people age, there is also increasing variability in individually calculated pharmacokinetic parameters, such that the clearance of drugs may vary greatly among elderly patients [10].

TABLE 25.3. Hepato-renal changes with aging.

Hepatic	Decreased liver size Decreased perfusion Decreased synthetic and metabolic capacity
Renal	Decreased renal tissue mass Decreased perfusion Decreased glomerular filtration rate and functional reserve Decreased creatinine clearance Decreased response to antidiuretic hormone Decreased ability to conserve sodium or concentrate urine Increased number of nonfunctional glomeruli Increased susceptibility to renal ischemia and renal failure

Nervous System

As with other aspects of senescence, cognitive function shows a great deal of variation in terms of baseline deficit and reserve. Recent data have highlighted the association between postoperative delirium and long-term outcome, underscoring the concept that even short-term cognitive impairment may reflect more systemic deficits. While there are considerable data regarding postoperative delirium in cardiac surgical patients subject to micro-embolic insults to the brain as the result of manipulation of the heart and aorta [11], other reports have focused on implications in noncardiac surgical patients. Robinson et al. [12] recently published a study of 144 patients over the age of 50 – of which over half underwent noncardiac thoracic surgery – that found a 44% incidence of delirium when a series of functional and cognitive assessments were carefully applied. The average time to onset was 2.1 ± 0.9 days with a duration of 4.0 ± 5.1 days. Risk factors included increasing age, hypoalbuminemia, anemia, intraoperative hypotension, history of alcohol abuse, and comorbid conditions, along with pre-existing dementia and impaired functional status. Importantly, the presence of delirium was associated with an increased length of hospital stay, a higher incidence of postdischarge institutionalization, and a greater 6-month mortality.

Aging and the Thoracic Surgical Population

Although cancer can occur at any age, it disproportionately strikes the elderly. Cancer is the leading cause of death among people age 60–79, and the second leading cause of death in those age 80 and older [2]. Data indicate that persons older than 65 have a 9.8-fold increased incidence of cancer compared with those younger than 65 [3], and the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program revealed that 56% of all newly diagnosed cancer patients were over 65 years of age [1]. Consistent with the overall aging of the population and the trend toward increasing age at the time of cancer diagnosis is an increase in the absolute number of elderly patients presenting with potentially resectable malignancy. For lung cancer in particular, the median age of patients presenting for surgical resection is now in excess of 70 years [2].

Other factors are also increasing the number of aged patients undergoing surgical treatment. For example, projections suggest that the incidence of lung cancer in women will soon equal that of men with a presumptive increase in the number of elderly women presenting for lung resection [13]. Similarly, neoadjuvant chemotherapy and radiation in patients with locally advanced stage III nonsmall cell lung cancer (NSCLC) are expanding the range of patients who are candidates for surgical resection. Support for this trend can be found in studies that demonstrated a significant survival

advantage in patients undergoing preoperative chemotherapy followed by surgery compared to those undergoing surgery alone [14–18]. Emerging data suggests that even elderly patients who receive neoadjuvant therapy for esophageal cancer do not have significantly increased mortality or major complications after esophagectomy despite the insult of both laparotomy and thoracotomy [19].

The Risk–Benefit Relationship of Surgical Intervention in the Elderly

Surgical resection remains the treatment of choice for early-stage lung cancer, yet several reports have presented variable results for resection in the elderly. Based on these data and the fact that the elderly will present with significant comorbidities, clinicians have traditionally offered less aggressive treatment to this group, with some even recommending a non-operative approach or less than an anatomic resection. However, advances in perioperative care and in surgical technique have now encouraged many to offer surgical resection to the aged population. Ultimately, the fundamental question for many patients is how the risk of surgery compares to that of other interventions or no intervention at all. Current data indicate that at initial diagnosis elderly patients tend to have earlier stage lung cancer than younger patients [20]. In addition, they tend to have a higher incidence of squamous cell lung cancers with a clinically reduced growth rate and metastatic

potential. Nonetheless, these data need to be interpreted in the context of operative risk and what “long term” may mean to an 85-year-old.

Age-Related Perioperative Morbidity and Mortality

For patients aged ≥ 70 , Birim et al. [21] concluded from a retrospective study that operative morbidity and mortality are low enough to justify pulmonary resection for cancer. In this population, surgery was associated with a hospital mortality rate of 3.2% (relative to the common rate of $\sim 1.5\%$ reported for patients less than 65) along with minor and major complication rates of 51 and 13%, respectively, the most frequent events being arrhythmia (31%) and air leak lasting >5 days (21%). Five and 10-year survival rates were 37 and 15%, respectively, with smoking, COPD, and pathologic stage significant risk factors in overall survival. In patients age 80 and older, data from The Lung Cancer Study published in 1983 indicate that rates of complication and mortality for octogenarians are substantially higher than for the under 65 group (mortality rate of 8.1 vs. 1.6%) [22]. However, more recent studies suggest improvement in the results of lung resection in octogenarians [23–26]. In 1998, the Japanese Association of Chest Surgery reported a mortality rate of only 2.2% in a sample of 225 octogenarians undergoing lung cancer resection [27], while other series [28–33] found a mortality of less than 5% (Table 25.4). Results of a retrospective cohort study of 68 octogenarians

TABLE 25.4. Reported morbidity and mortality with surgical resection in the elderly.

Source	Number of patients	Procedures	Morbidity (minor and major) (%)	Mortality (%)	Mean age
Onaitis et al. [28]	500	VATS lobectomy	20	1.2	65
McKenna et al. [29]	1,100	VATS lobectomy	15.3	0.8	71
McVay et al. [30]	159	VATS153 Lobectomy 3 Bilobectomy 3 Pneumonectomy 3	18	1.8	83
Matsuoka et al. [31]	40	16 lobectomy 12 segmentectomy 12 wedge resections	20	0	82
Port et al. [32]	61	46 lobectomy 6 segmentectomy 5 wedge resections 4 pneumonectomy	38	1.6	82
Brock et al. [33]	68	47 lobectomy 11 wedge resections 5 segmentectomy 4 bilobectomy 1 pneumonectomy	44	8.8	82
Koizumi et al. [59]	32	17 VATS lobectomy 15 thoracotomy lobectomy	56	12.5	82
Aoki et al. [67]	35	25 standard or extended lobectomy 10 wedge resections	60	0	80
Pagni et al. [40]	54	43 lobectomy 2 extended lobectomy 2 bilobectomy 3 segmentectomy 3 wedge resections 1 pneumonectomy	42	3.7	82

with NSCLC who underwent lung resection reinforced that health status and tumor stage are more important than chronologic age with regard to outcome and survival rate [31]. In this study, ASA classification, forced expiratory volume in 1 s (FEV1) of less than 1.5 L, and stage of disease were strong, independent predictors of long-term survival. Similarly, in a study of octogenarians who were offered surgical resection, the mortality was 1.6% and overall 5-year survival for stage 1a patients was 82% [32]. Somewhat surprisingly, several recent studies of patients undergoing esophagectomy for esophageal cancer report that outcomes for elderly patients, including mortality, postoperative complications, and long-term results, are also similar to those for younger patients [34–39].

Risk and Oncological Outcome

Compared to a younger patient, an elderly person may value different goals of therapy. As the risks of surgical intervention increase along with severity of comorbid conditions, the patient's priorities may shift. Long-term survival may become less important than relief of symptoms, quality of life, and maintaining level of functioning. Accordingly, elderly patients may be less inclined to accept the risks of a major surgery, even if it might be curative, in favor of less invasive alternatives [4]. However, there being such variation in functional status among elderly patients, major surgical procedures that are potentially curative may be perfectly reasonable for many patients particularly when considered in light of data suggesting that average life expectancies for 70-year-old men and women are currently an additional 12.5 and 15.3 years, respectively. For 85-year-old men and women, they may expect an additional 5.3 and 6.3 years, respectively, and even the 100-year-old person may expect an additional 2 years of life, on average [40, 41]. Nonetheless, with increasing age, the absolute gain in life expectancy from surgical treatment clearly diminishes. However, the life expectancy among patients with lung cancer that is not surgically managed is so low that resection for an 85-year-old patient may still result in an appreciable prolongation of life. For example, impression that the life expectancy of an octogenarian with lung cancer is limited by death from natural causes is not supported by the US census data. In fact, the average life expectancy for an 80-year-old living in the United States is now an impressive 8.6 years. This translates into an overall 5-year survival for an age-matched population of 80%, as calculated from life tables. Furthermore, the majority of this time is anticipated to be years of active and independent life. Given these facts, it seems likely that the greatest impact on an elderly patient's survival and quality of life would be their cancer-related mortality rather than their age. This prospect is highlighted by the results of a retrospective review of 49 patients with early stage disease who either refused surgery or whose comorbid conditions rendered surgery unreasonable and experienced a survival time of only 14 months [42]. A meta-analysis of patients enrolled in trials for computed tomography screening that did not receive surgical therapy for their stage I disease

produced similar findings [43], and a study of elderly subjects with stage I and II NSCLC receiving radiation alone revealed 2- and 5-year survival rates of only 40 and 16%, respectively [44]. On the whole, these data indicate that early stage lung cancer is a fatal disease, and suggest that for patients with lung cancer who are over 80 years old, the majority of deaths will be related to the progression of lung cancer rather than other causes.

The Emerging Role of Minimally Invasive Surgical (MIS) Techniques

In that there is an association between the magnitude of pulmonary resection and postoperative complications in elderly subjects, some surgeons advocate "less invasive" lung-sparing techniques such as wedge resection and segmentectomy for the treatment of pulmonary malignancy whenever possible [45]. While controversy exists as to whether these procedures, which still involve at least a limited thoracotomy, carry a higher risk of local recurrence, Mery et al., using data from the SEER database, found that, among patients age 75 or older, there was no difference in overall survival time between patients undergoing lobectomy and those undergoing limited resection [20].

Both the scientific literature and lay press contain a wide variety of publications relating to VATS as a truly "minimally invasive" approach to the treatment of lung cancer and as an adjunct in the treatment of esophageal cancer. Published data suggest that relative to thoracotomy, VATS patients experience shorter chest tube duration, shorter postoperative hospital stays, lower narcotic requirements for postoperative pain, and reduced shoulder dysfunction [46]. Similarly, patients who had VATS lobectomy reported less postoperative pain, decreased time until return to preoperative activities, and higher satisfaction with the results of surgery than those patients undergoing conventional thoracotomy [47]. In addition, there was a lower observed incidence of postoperative confusion [48], which has been associated with increased postoperative morbidity and mortality. VATS lobectomy patients also appear to return to their oncologists for adjuvant chemotherapy more readily. A recent review of 1,100 VATS lobectomies with either lymph node sampling or dissection for patients with a mean age of 71.2 years demonstrated low rates of mortality (<1%) and morbidity, with 84.7% of patients exhibiting no significant complications [29]. For esophagectomy, several minimally invasive approaches have been developed, including those incorporating thoracoscopy and/or laparoscopy into a typical three stage Ivor Lewis operation, approaches incorporating laparoscopy for a transhiatal approach, and those incorporating robotics. Emerging data support the oncological efficacy of these approaches [49, 50]. Galvani et al. reported experiences with robotically assisted laparoscopic transhiatal esophagectomy, suggesting that this approach is safe and effective [51].

Despite favorable perioperative outcome data, questions remain as to whether lobectomy via thoracotomy and VATS

are equivalent therapeutic interventions for cancer. However, a series of 159 VATS lobectomies for stage I and II NSCLC revealed long-term outcomes and local recurrence rates that were at least equivalent to those of open thoracotomy [52], and a prospective, randomized trial of 100 patients with stage IA NSCLC concluded that long-term survival and local recurrence rates after VATS lobectomy were comparable to those for open thoracotomy [53]. Another study actually reported better 5-year survival rate of Stage I lung cancer after VATS vs. thoracotomy perhaps due in part to superior postoperative pulmonary function [54]. Several other studies reported similar outcomes [55–58]. For the geriatric population, a retrospective study of 32 lobectomy patients aged 80 years or older (17 VATS, 15 thoracotomies) also demonstrated better 5-year survival following VATS [59]. A recent review of our own data related to VATS lobectomy in octogenarians revealed that 31 patients had a significantly decreased length of ICU and hospital stay as well as a decreased complication rate. Interestingly, significantly fewer patients required discharge to a formal rehabilitation center and were discharged to home.

To date, most large reports show that across all age groups VATS for lobectomy is safe, with morbidity rates in some reports lower than seen historically with thoracotomy. Other data suggest that pulmonary function as measured by vital capacity and FEV1 may be better preserved in patients undergoing VATS rather than thoracotomy [54]. Kirby et al. [60] reported that, while they found no difference in intraoperative time, blood loss, or length of hospital stay between patients who underwent VATS vs. thoracotomy, the thoracotomy group did experience significantly more postoperative complications, most notably prolonged air leaks.

The prospect of superior pulmonary function following VATS relative to thoracotomy has particular significance in the elderly population. To determine if the VATS approach for lobectomy offers specific advantages over thoracotomy in the elderly, retrospective studies have compared the two in aged patient populations. Jaklitsch reported that VATS procedures for patients ≥ 65 years of age resulted in superior 30-day operative mortality, which was essentially unrelated to age, and a decreased length of hospital stay compared to previous reports for standard thoracotomy [48]. More recently, Cattaneo et al. analyzed the incidence and grade of postoperative complications in patients ≥ 70 years of age undergoing a VATS approach vs. a thoracotomy for lobectomy [61]. The two groups were identically matched for age, gender, comorbidities, and clinical stage. This study found that VATS resulted in a lower overall complication rate, less pulmonary morbidity, and a decreased median length of stay. In addition, the severity of complications were less in the VATS group, suggesting that the minimally invasive approach can lead to better tolerance in a high-risk, elderly population.

Whether there are cardiovascular benefits to VATS lobectomy remains unclear. Multiple studies have established the relationship between age and the occurrence of atrial fibrillation following lobectomy, with recent data indicating an incidence of

27% in patients over the age of 60 when continuous telemetry is used for diagnosis [62]. Two large series have reported lower than expected rates of postoperative atrial fibrillation following VATS lobectomy relative to thoracotomy, ranging from 2.9 to 10% [28, 29]. However, neither study used routine postoperative telemetry in the highest risk patients, i.e., elderly patients, and likely underreported asymptomatic episodes of atrial fibrillation. In contrast, a matched, case–control study by Park et al. comparing 244 patients undergoing lobectomy by either VATS or thoracotomy [63] showed no difference in the rate of postoperative atrial fibrillation with VATS patients exhibiting a 12% rate of postoperative atrial fibrillation compared to 16% for thoracotomy patients ($p=0.36$). Predictably, in both groups patients experiencing atrial fibrillation were significantly older (median 72 years) than those who did not develop the arrhythmia (median 66 years).

Preoperative Evaluation and Postoperative Care

Although the fundamentals of preoperative evaluation outlined elsewhere in the text remain appropriate, aspects of perioperative assessment and planning take on increased importance and/or require different interpretation in the elderly.

Preoperative Assessment

Current guidelines developed by the American College of Chest Physicians for preoperative assessment of patients considered for thoracic surgery begins with a physical exam combined with cardiovascular evaluation and spirometry [64]. Given the lung parenchymal changes associated with aging and propensity for obstructive physiology, measurement of diffusion capacity (DLCO) is important, particularly for patients with clinical signs of dyspnea out of proportion to the spirometry results. In patients with an FEV1 or DLCO $<80\%$ of predicted – a relatively common finding in the elderly – estimated postoperative FEV1 and DLCO values should be calculated as described in Chap. 2. Estimated postoperative values for either variable of $<40\%$ is a significant negative predictor of outcome in all patients, and may be even more relevant in the aged due to the expected changes in intrinsic pulmonary reserve associated with senescence. Importantly, results need to be interpreted in the context of a patient’s clinical presentation; a low FEV1 in a patient with a large left mainstem bronchus tumor should be regarded differently than a patient who has a similarly low value and a small peripheral lesion.

Guidelines suggest that further definition of a patient’s risk with cardiopulmonary exercise testing and estimation of maximal oxygen consumption (VO_2 max) is often valuable. A VO_2 max <15 mL/kg/min is a negative predictor for outcome. If cardiopulmonary exercise testing is not available other surrogates can be performed and include stair climbing, shuttle walk, and

the 6 min walk. If a patient cannot climb one flight of stairs or perform 25 shuttles, usually their VO_2 max will be $<10 \text{ mL/kg/min}$. However, while exercise testing is a potentially powerful tool, it is not always applicable in the geriatric population due to the presence of comorbidities such as arthritis or peripheral vascular disease that limit mobility independent of VO_2 max.

In the elderly population, it is also important to identify factors such as dementia, undernutrition, thromboembolic disorders, subclinical diabetes, thyroid disorders, and renal insufficiency. For many patients, perioperative risk can be reduced by modest exercise along with nutritional and hormonal optimization. However, unlike recommendations published nearly 20 years ago suggesting 8 weeks of optimization prior to surgery [65], in the current environment, and in the setting of progressive malignancy, the time available for meaningful preoperative optimization is often quite short.

Postoperative Planning

In the absence of severe pre-existing critical illness or profound intraoperative complications, diagnostic and staging procedures such as bronchoscopy, cervical mediastinoscopy, and potentially even minimally invasive wedge biopsies may be performed as outpatients, even in elderly patients. Following VATS or open lobectomy and even pneumonectomy, elderly patients generally are candidates for standard admission to postoperative acute care units [66]. Alternatively, after more extensive procedures such as bilobectomy, esophagectomy, or resection of a large or adherent mediastinal mass, ICU admission is often desirable due to the increased potential for major respiratory and cardiovascular postoperative complications.

It is also important to consider discharge planning even during the initial preoperative visit in the elderly population. For example, it is necessary to consider who will be providing support for the patient following discharge, and where this care will take place. Many patients who are entirely self-sufficient preoperatively may not be able to care for themselves for a period of time postoperatively, and as such, early discharge planning becomes critical.

Conclusion

As the population ages, increasing numbers of elderly people will present with lung cancer. Due to recent advances in neoadjuvant therapies and accumulating data demonstrating a favorable risk–benefit relationship even in octogenarians, more of these geriatric patients will be surgical candidates. Within this aged population, there are often wide disparities between chronologic age and physiologic condition, which is underscored by data indicating that outcome is influenced more by tumor stage, preoperative functional status and comorbidities than age alone. Nonetheless, the normal process of cardiopulmonary aging can serve to limit the physiological reserve necessary to compensate for perioperative stress even

in otherwise healthy elderly patients. Emerging experience now also suggests that minimally invasive surgical techniques for the treatment of lung cancer may parallel conventional thoracotomy in terms of oncologic efficacy while decreasing perioperative morbidity in the elderly. Accordingly, for anesthesiologists, the future may hold the prospect of caring for very old, ill patients undergoing minimally invasive thoracic surgery.

Clinical Case Discussion

Case: An 84-year-old male presented with a left lung mass on a chest radiograph obtained during evaluation for right total knee replacement. Transthoracic biopsy was performed, and the mass found to be nonsmall cell lung carcinoma (NSCLC). Imaging studies revealed hilar adenopathy, and lymph nodes obtained from the left chest by mediastinoscopy were positive for NSCLC leading to disease classification as stage III A. He subsequently underwent induction chemotherapy. Recent evaluation shows a decrease in size of the mass and regression of hilar adenopathy.

The patient is now scheduled for VATS resection of the left upper lung lobe. His medical history is otherwise notable for past smoking (none for 20 years), daily alcohol consumption (2–3 glasses of wine), hypertension (controlled), hypercholesterolemia, and severe osteoarthritis of the right knee (he had previously undergone left total replacement at age 78). Preoperative evaluation has been remarkable for anemia (hematocrit 33%), mild COPD, and a dobutamine stress echocardiogram negative for ischemia (mobility limited by knee pain and instability). On physical exam he appears fit and vigorous but limited to a wheelchair when walking more than a block due to knee instability. He states that his plan is to proceed with knee replacement surgery following recovery from the lobectomy.

Questions

1. Is lung resection an acceptable approach for this patient from a physiological perspective?
2. Is left upper lobe lobectomy an acceptable procedure for this patient from an oncological standpoint?
3. What types of complications might this patient be at risk of developing?
4. What are some possible advantages of performing this procedure using video-assisted thoracoscopy?

Discussion

1. While this patient may appear to be fit and vigorous at baseline, all elderly patients have altered physiology as a consequence of aging. Thus, the stress of surgery may unmask these decreased functional reserves. For example, this patient may exhibit diminished maximum voluntary

ventilation in response to the carbon dioxide load created by shivering, thus putting him at increased risk for hypercarbia in the postoperative period. Other alterations in respiratory function associated with aging, such as decreased PaO_2 , decreased DLCO, and increased ventilation-perfusion mismatch may increase the patient's risk of hypoxia.

Although this patient's dobutamine stress echocardiogram was negative for ischemia, his advanced age suggests that he has some degree of LV hypertrophy and slower myocardial relaxation, which could negatively affect cardiac filling in the setting of tachycardia, for example.

These changes should be kept in mind during the perioperative period. However, a patient with good functional status, even an 84-year-old, can undergo this procedure safely.

2. Lung cancer is a fatal disease, with an estimated 5-year survival rate of 16% without surgical resection. Thus, a patient with good functional status stands to gain survival time if his stage I lung cancer is resected, even at an advanced age. This patient underwent induction chemotherapy for stage IIIA cancer, which caused regression of his adenopathy and decreased tumor size. Recent studies suggest that such patients stand to benefit from lung resection after chemotherapy, experiencing increased survival time.
3. Any patient undergoing lobectomy is at risk for cardiovascular and respiratory complications. Arrhythmias such as atrial fibrillation are among the most common complications, but myocardial ischemia, and bleeding may also occur. Pneumonia and respiratory failure, prolonged air-leak, bronchopleural fistula and empyema are also possible risks in the setting of pulmonary surgery. However, preoperative health status, a history of COPD or smoking, and tumor stage all seem to contribute to outcome more than chronological age does.
4. VATS may result in better outcomes than thoracotomy. Recent data suggest that patients who underwent VATS as compared to patients who underwent thoracotomy experienced shorter hospital stays, less postoperative pain, less postoperative confusion, decreased time to return of preoperative activities, higher satisfaction with the results of surgery. Several studies have reported decreased postoperative complication rates with the use of VATS rather than thoracotomy for lobectomy, which may be related to better preserved pulmonary function following minimally invasive surgery. Mortality rates were also significantly better for patients who underwent VATS, regardless of age.

References

1. Yancik R. Population aging and cancer: a cross-national concern. *Cancer J.* 2005;11(6):437–41.
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. *CA Cancer J Clin.* 2009;59(4):225–49.
3. Hurria A, Kris MG. Management of lung cancer in older adults. *CA Cancer J Clin.* 2003;53(6):325–41. Review.
4. Watters JM, McClaran JC, Man-Son-Hing M. The elderly surgical patient. In: ACS surgery principles and practice. New York, NY: WebMD; 2005.
5. Sieber FE, Paulding R. Geriatric anesthesia. In: Miller RD, editor. *Anesthesia*. Philadelphia: Churchill Livingstone; 2009.
6. Lakatta EG, Sollott SJ. Perspectives on mammalian cardiovascular aging: humans to molecules. *Comp Biochem Physiol A Mol Integr Physiol.* 2002;132(4):699–721.
7. Castillo MD, Heerd PM. Lung resection in the elderly. *Curr Opin Anaesthesiol.* 2007;20(1):4–9.
8. Levitzky MG. Alveolar ventilation. McGraw-Hill: In *Respiratory Physiology*; 2007.
9. Epstein M. Aging and the kidney. *J Am Soc Nephrol.* 1996;7: 1106–22.
10. Muhlberg W, Platt D. Age-dependent changes of the kidneys: pharmacological implications. *Gerontology.* 1999;45(5):243–53.
11. Katzenbach R, Djaiani GN, Borger MA, et al. Preoperative use of statins is associated with reduced early delirium rates after cardiac surgery. *Anesthesiology.* 2009;110(1):67–73.
12. Robinson TN, Raeburn CD, Tran ZV, et al. Postoperative delirium in the elderly: risk factors and outcomes. *Ann Surg.* 2009;249(1):173–8.
13. Neugut AI, Jacobson JS. Women and lung cancer: gender equality at a crossroad? *JAMA.* 2006;296(2):218–9.
14. Roth JA, Atkinson EN, Fossella F, et al. Long-term follow-up of patients enrolled in a randomized trial comparing preoperative chemotherapy and surgery with surgery alone in resectable stage IIIA non-small-cell lung cancer. *Lung Cancer.* 1998;21:1–6.
15. Takeda S, Maeda H, Okada T, et al. Results of pulmonary resection following neoadjuvant therapy for locally advanced (IIIA-IIIB) lung cancer. *Eur J Cardiothorac Surg.* 2006;30(1):184–9.
16. Rosell R, Gomez-Codina J, Camps C, et al. Preresectional chemotherapy in stage IIIA non-small-cell lung cancer a 7-year assessment of a randomized controlled trial. *Lung Cancer.* 1999; 26:7–14.
17. Fujita S, Katakami N, Takahashi Y, et al. Postoperative complications after induction chemoradiotherapy in patients with non-small-cell lung cancer. *Eur J Cardiothorac Surg.* 2006;29(6):896–901.
18. Petersen RP, Pham D, Toloza EM, et al. Thoracoscopic lobectomy: a safe and effective strategy for patients receiving induction therapy for non-small cell lung cancer. *Ann Thorac Surg.* 2006;82(1):214–8.
19. Ruol A, Portale G, Castoro C, et al. Effects of neoadjuvant therapy on perioperative morbidity in elderly patients undergoing esophagectomy for esophageal cancer. *Ann Surg Oncol.* 2007;14(11):3243–50.
20. Mery CM, Pappas AN, Bueno R, et al. Similar long-term survival of elderly patients with non-small cell lung cancer treated with lobectomy or wedge resection within the Surveillance, Epidemiology, and End Results Database. *Chest.* 2005;128:237–45.
21. Birim O, Zuydendorp HM, Maaat AP, et al. Lung resection for non-small-cell lung cancer in patients older than 70: mortality, morbidity, and late survival compared with the general population. *Ann Thorac Surg.* 2003;76(6):1796–801.
22. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg.* 1983;86:654–8.
23. Yamamoto K, Alarcon JP, Medina VC, et al. Surgical results of stage I non-small cell lung cancer: comparison between elderly and younger patients. *Eur J Cardiothorac Surg.* 2003;23(1):21–5.

24. Sullivan V, Tran T, Holmstrom A, et al. Advanced age does not exclude lobectomy for non-small cell lung carcinoma. *Chest*. 2005;128(4):2671–6.
25. Sawada S, Komori E, Nogami N, et al. Advanced age is not correlated with either short-term or long-term postoperative results in lung cancer patients in good clinical condition. *Chest*. 2005;128:1557–63.
26. Hanagiri T, Muranaka H, Hashimoto M, et al. Results of surgical treatment of lung cancer in octogenarians. *Lung Cancer*. 1999;23(2):129–33.
27. Wada H, Nakamura T, Nakamoto K, et al. Thirty-day operative mortality for thoracotomy in lung cancer. *J Thorac Cardiovasc Surg*. 1998;115:70–3.
28. Onaitis MW, Petersen RP, Balderson SS, et al. Thoracoscopic lobectomy is a safe and versatile procedure: experience with 500 consecutive patients. *Ann Surg*. 2006;244(3):420–5.
29. McKenna Jr RJ, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1, 100 cases. *Ann Thorac Surg*. 2006;81(2):421–5.
30. McVay CL, Pickens A, Fuller C, et al. VATS anatomic pulmonary resection in octogenarians. *Am Surg*. 2005;71(9):791–3.
31. Matsuoka H, Okada M, Sakamoto T, Tsubota N. Complications and outcomes after pulmonary resection for cancer in patients 80 to 89 years of age. *Eur J Cardiothorac Surg*. 2005;28(3):380–3.
32. Port JL, Kent M, Korst RJ, et al. Surgical resection for lung cancer in the octogenarian. *Chest*. 2004;126(3):733–8.
33. Brock MV, Kim MP, Hooker CM, et al. Pulmonary resection in octogenarians with stage I nonsmall cell lung cancer: a 22-year experience. *Ann Thorac Surg*. 2004;77(1):271–7.
34. Internullo E, Moons J, Nafteux, et al. Outcome after esophagectomy for cancer of the esophagus and GEJ in patients aged over 75 years. *Eur J Cardiothorac Surg*. 2008;33(6):1096–104.
35. Perry Y, Fernando HC, Buenaventura PO, et al. Minimally invasive esophagectomy in the elderly. *JSLS*. 2002;6(4):299–304.
36. Nguyen NT, Hinojosa MW, Smith BR, et al. Minimally invasive esophagectomy: lessons learned from 104 operations. *Ann Surg*. 2008;248(6):1081–91.
37. Ruol A, Portale G, Zaninotto G, et al. Results of esophagectomy for esophageal cancer in elderly patients: age has little influence on outcome and survival. *J Thorac Cardiovasc Surg*. 2007;133(5):1186–92.
38. Morita M, Egashira A, Yoshida R, et al. Esophagectomy in patients 80 years of age and older with carcinoma of the thoracic esophagus. *J Gastroenterol*. 2008;43(5):345–51.
39. Alibakhshi A, Aminian A, Misharifi R, et al. The effect of age on the outcome of esophageal cancer surgery. *Ann Thorac Med*. 2009;4(2):71–4.
40. Pagni S, McKelvey A, Riordan C, et al. Pulmonary resection for malignancy in the elderly: is age still a risk factor? *Eur J Cardiothorac Surg*. 1998;14(1):40–4.
41. Ventura SJ, Peters KD, Martin JA, et al. Births and deaths: United States, 1996. *Mon Vital Stat Rep*. 1997;46(1 Suppl 2):1.
42. McGarry RC, Song G, des Rosiers P, et al. Observation-only management of early stage, medically inoperable lung cancer: poor outcome. *Chest*. 2002;121:1155–8.
43. Flehinger BJ, Kimmel M, Melamed MR. The effect of surgical treatment on survival from early lung cancer: implications for screening. *Chest*. 1992;101:1013–8.
44. Furuta M, Hayakawa K, Katano S, et al. Radiation therapy for stage I-II non-small cell lung cancer in patients aged 75 years and older. *Jpn J Clin Oncol*. 1996;26:95–8.
45. Wiener DC, Argote-Greene LM, Ramesh H, et al. Choices in the management of asymptomatic lung nodules in the elderly. *Surg Oncol*. 2004;13(4):239–48. Review.
46. Landreneau RJ, Hazelrigg SR, Mack MJ, et al. Postoperative pain-related morbidity: video-assisted thoracic surgery versus thoracotomy. *Ann Thorac Surg*. 1993;56(6):1285–9.
47. Sugiura H, Morikawa T, Kaji M, et al. Long-term benefits for the quality of life after video-assisted thorascopic lobectomy in patients with lung cancer. *Surg Laparosc Endosc Percutan Tech*. 1999;9(6):403–8.
48. Jaklitsch MT, DeCamp MM, Liptay MJ, et al. Video-assisted thoracic surgery in the elderly. A review of 307 cases. *Chest*. 1996;110:751–8.
49. Schoppmann SF, Prager G, Langer F, et al. Fifty-five minimally invasive esophagectomies: a single centre experience. *Anticancer Res*. 2009;29(7):2719–25.
50. Braghetto I, Csendes A, Cardemil G, et al. Open transthoracic or transhiatal esophagectomy versus minimally invasive esophagectomy in terms of morbidity, mortality and survival. *Surg Endosc*. 2006;20(11):1681–6.
51. Galvani CA, Goodner MV, Moser F, et al. Robotically assisted laparoscopic transhiatal esophagectomy. *Surg Endosc*. 2008;22(1):188–95.
52. Walker WS, Codispoti M, Soon SY, et al. Long-term outcomes following VATS lobectomy for non-small cell bronchogenic carcinoma. *Eur J Cardiothorac Surg*. 2003;23(3):397–402.
53. Sugi K, Kaneda Y, Esato K. Video-assisted thoracoscopic lobectomy achieves a satisfactory long-term prognosis in patients with clinical stage IA lung cancer. *World J Surg*. 2000;24(1):27–30.
54. Kaseda S, Aoki T, Hangai N, Shimizu K. Better pulmonary function and prognosis with video-assisted thoracic surgery than with thoracotomy. *Ann Thorac Surg*. 2000;70(5):1644–6.
55. Daniels LJ, Balderson SS, Onaitis MW, D'Amico TA. Thoracoscopic lobectomy: a safe and effective strategy for patients with stage I lung cancer. *Ann Thorac Surg*. 2002;74(3):860–4.
56. Thomas P, Doddoli C, Yena S, et al. VATS is an adequate oncological operation for stage I non-small cell lung cancer. *Eur J Cardiothorac Surg*. 2002;21(6):1094–9.
57. Ohtsuka T, Nomori H, Horio H, et al. Is major pulmonary resection by video-assisted thoracic surgery an adequate procedure in clinical stage I lung cancer? *Chest*. 2004;125(5):1742–6.
58. Gharagozloo F, Tempesta B, Margolis M, Alexander EP. Video-assisted thoracic surgery lobectomy for stage I lung cancer. *Ann Thorac Surg*. 2003;76:10009–15.
59. Koizumi K, Haraguchi S, Hirata T, et al. Lobectomy by video-assisted thoracic surgery for lung cancer patients aged 80 years or more. *Ann Thorac Cardiovasc Surg*. 2003;9(1):14–21.
60. Kirby TJ, Mack MJ, Landreneau RJ, Rice TW. Lobectomy-video-assisted thoracic surgery versus muscle-sparing thoracotomy: a randomized trial. *J Thorac Cardiovasc Surg*. 1995;109:997–1002.
61. Cattaneo SM, Park BJ, Wilton AS, et al. Use of video-assisted thoracic surgery for lobectomy in the elderly results in fewer complications. *Ann Thorac Surg*. 2008;85(1):231–5.
62. Amar D, Zhang H, Heerd PM, et al. Statin use is associated with a reduction in atrial fibrillation after noncardiac thoracic surgery independent of C-reactive protein. *Chest*. 2005;128(5):3421–7.
63. Park BJ, Zhang H, Rusch VW, Amar D. Video-assisted thoracic surgery does not reduce the incidence of postoperative atrial fibrillation after pulmonary lobectomy. *J Thorac Cardiovasc Surg*. 2007;133:775–9.

64. Colice GL, Shafazand S, Griffin JP, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidence-based clinical practice guidelines (2nd edition). College of Chest Physicians. *Chest*. 2007;132 (3 Suppl):161S–77.
65. King MS. Preoperative evaluation of the elderly. *J Am Board Fam Pract*. 1991;4(4):251–8.
66. Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care unit versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22(1):50–5.
67. Aoki T, Yamato Y, Tsuchida M, et al. Pulmonary complications after surgical treatment of lung cancer in octogenarians. *Eur J Cardiothorac Surg*. 2000;18(6):662–5.

Thoracic Anesthesia for Morbidly Obese Patients and Obese Patients with Obstructive Sleep Apnea

Jay B. Brodsky

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Key Points

- Body mass index (BMI) (BMI = Weight_{kilograms} / (Height_{meters})²) is a measure of obesity. A patient with a BMI >30 kg/m² is obese, and >40 kg/m² morbidly obese (MO). Morbid obesity is associated with medical conditions including hypertension, type II diabetes, cardiac disease, and obstructive sleep apnea (OSA).
- Moderate to severe OSA is present in more than 50% of MO patients, and is often unrecognized. Definitive diagnosis is made by polysomnography (PSG). In the absence of PSG documentation, all MO patients should be managed as if they have OSA. The ASA Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea should be used for all MO patients, whether or not they have had a PSG diagnosis of OSA.
- The best preoperative predictors of potential problems with tracheal intubation in MO patients are high Mallampati (III or IV) score and increased neck circumference (>48 cm men, >40 cm women). Many MO are difficult to ventilate by face mask, but the majority have no difficulty undergoing direct laryngoscopy and tracheal intubation.
- Never allow a supine MO patient to breathe without assistance. A MO patient should be positioned in the head-elevated laryngoscopy position (HELP) prior to anesthetic induction. In this position, the patient's head and upper body are ramped or "stacked" so that an imaginary horizontal line

can be drawn from the sternum to the ear. If the patient is hemodynamically stable, the operating room table should also be in a reverse-Trendelenburg position (RTP) to maximize "safe apnea time."

- MO patients tolerate one-lung ventilation (OLV) in the lateral position. Although there are no clinical studies of OLV in supine MO patients, in theory a MO patient would not be expected to tolerate OLV this position.
- A MO OSA patient using a continuous positive airway pressure (CPAP) device preoperatively should bring their equipment to the hospital for use during their postoperative recovery.
- Depressant medications can decrease ventilatory responsiveness to hypoxemia and hypercarbia in all MO patients, and can also cause airway collapse in OSA patients. Avoid sedative premedication and long-lasting opioids since both increase the risk of postoperative ventilatory problems. Use regional techniques when possible. For postoperative analgesia, use multimodal analgesic therapy (local anesthetics for epidural, spinal and paravertebral analgesia, nonsteroidal anti-inflammatory agents, and alpha-2 agonists (clonidine, dexmedetomidine)) to reduce the need for opioids.
- Following any long-duration operation check the patient's serum for creatinine phosphokinase (CPK). A CPK level >1,000 IU/L is diagnostic for rhabdomyolysis (RML). The initial symptoms of RML (numbness, pain, weakness) can be masked, especially if epidural analgesia is being used.

Introduction

As a consequence of the current worldwide obesity epidemic, extremely obese patients now routinely undergo the entire gamut of surgery, including thoracic operations [1]. Obese patients differ from their normal-weight counterparts due to alterations in their anatomy and physiology, and because they often have significant additional comorbid medical conditions that can complicate their operative course and increase the risks of postoperative problems. One of the conditions frequently associated with extreme obesity is obstructive sleep apnea (OSA), a condition that further adds to the complexity of managing an obese patient. This chapter will consider the perioperative anesthetic care of the morbidly obese (MO) patient undergoing thoracic surgery. Published studies of obese and MO thoracic surgical patients are almost nonexistent, so most of the discussion is based on experience with similar patients undergoing other types of surgery, particularly weight loss operations.

Definitions

Obesity

Obesity is a relative term that can have different definitions in different cultures depending on societal norms. Medically, obesity is usually described by BMI. BMI is calculated by dividing the patient's weight (kilograms, kg) by the square of their height (meters, m) or $BMI = \frac{kg}{m^2}$. It is generally accepted that anyone with a BMI between 25 and 29 kg/m^2 is overweight, and obese if their BMI is $\geq 30 kg/m^2$. BMI itself is an indirect estimation of obesity since it considers any increase in weight as due to an increase in adipose tissue only.

Morbid obesity (MO) describes extreme obesity that, if untreated, will significantly shorten life expectancy. A variety of definitions exist, but a patient with a BMI $\geq 40 kg/m^2$ is considered to be MO. As a reflection of the worldwide obesity crisis, the term "super-obesity" has been introduced in the medical literature to describe patients with $BMI > 50 kg/m^2$. Based on these definitions, more than one third of American adults are obese and almost 5% are MO [2].

Weight

Anesthetic drugs are usually administered on the basis of either ideal body weight (IBW), lean body weight (LBW), or total body weight (TBW).

IBW is a measure initially derived by life insurance companies to describe the weight for a man or woman of a specific height that is statistically associated with maximum life expectancy. Ideal weight has increased over the past 4 decades since Americans are living longer despite significant increases in their average weight. IBW for calculation of drug dosing

can be simply estimated for both men and women by the formula, $IBW = (22)(m^2)$ [3].

In normal-weight patients TBW approximates IBW, that is, "normal" weight ranges between $\pm 10\%$ of IBW. LBW, which includes muscles, bones, tendons, ligaments, and body water, is equal to TBW minus the weight of body fat. LBW in nonobese patients should be about 80% TBW for males and 75% TBW for females. LBW and TBW both increase as a patient gets heavier since there is more muscle and body water in addition to more adipose tissue. LBW for a MO patient is estimated as $LBW_{obesity} = IBW + 20\text{--}30\%$.

Obstructive Sleep Apnea

Moderate to severe OSA is probably present in more than half the MO population, and the actual incidence may be even greater since OSA is frequently underdiagnosed [4]. OSA is characterized by repetitive collapse of the upper airway during sleep, which results in complete (apnea) or near complete cessation (hypopnea) of airflow.

Apnea is defined as a total lack of airflow lasting at least 10 s. Hypopnea is a decrease of $\geq 50\%$ in airflow or $\leq 50\%$ decrease for at least 10 s. These events are associated with either arousal from sleep and/or oxygen desaturation of $\geq 3\%$ [5]. If there is increasing respiratory effort the apnea is described as "obstructive," whereas in central sleep apnea there is no breathing effort [6]. Severe OSA is associated with sleep fragmentation, transient hypoxemia and hypercapnia, large negative intrathoracic pressure swings, and marked elevations in blood pressure [7].

Obesity Hypoventilation Syndrome

Obesity hypoventilation syndrome (OHS) is the combination of obesity ($BMI \geq 30 kg/m^2$) with sleep-disordered breathing (usually OSA) and chronic daytime hypercapnia ($PaCO_2 \geq 45 mmHg$) [4]. In its severest form, OHS has been termed "Pickwickian syndrome." In OHS there is a diminished central ventilatory drive despite elevated $PaCO_2$ [8]. Although OHS is rare in the general population, the incidence is estimated to be between 5 and 10% in MO OSA patients, with the greatest occurrence in super-obese patients.

Preoperative Assessment

A thorough preoperative assessment is indicated for any surgical patient. For the MO patient, the anesthesiologist must consider the many associated comorbid conditions (including hypertension and cardiovascular disease, type II diabetes, OSA and OHS, osteoarthritis), in addition to the medical indication for surgery. The specific approaches to each of the medical comorbidities associated with extreme obesity are beyond the scope of this chapter, and the reader is referred to reviews on this subject [9].

Airway

The patient's previous anesthesia records should be reviewed for evidence of any prior difficulties with tracheal intubation. A MO patient, especially one with a history or symptoms suggestive of OSA, may have a diminution of the pharyngeal space secondary to fat deposition in the pharyngeal wall which can make airway access and mask ventilation difficult. The patient's airway and anatomy should be closely examined. The best preoperative predictors of potential problems with tracheal intubation are Mallampati score (III/IV) and increased neck circumference [10].

Pulmonary Function

Excess body fat significantly reduces chest wall and total pulmonary compliance. Airway resistance and work of breathing are usually increased in the spontaneously breathing MO patient. Preoperatively, spirometry usually reveals a restrictive defect with decreases in functional residual capacity (FRC), mainly expiratory reserve volume (ERV), associated with small airway collapse during tidal breathing. These changes result in ventilation/perfusion (V/Q) mismatch, an elevated shunt fraction, and relative hypoxemia [11].

Preoperative pulmonary function testing has been useful for predicting which patient can safely undergo lung resection [12]. Published minimum values of at least 40% FEV₁ and 40% diffusion capacity may not be useful for the MO patient since measurements are not indexed to weight. No predictive baseline spirometry studies for MO patients undergoing lung resection have been published. However, as BMI increases postoperative FEV₁ and FVC values decrease proportionally [13]. For example, following abdominal surgery MO patients experience significantly more atelectasis, greater decreases in FRC, and lower PaO₂ values than matched normal-weight patients. Therefore, it is very likely, but still unproven, that MO patients also experience greater reductions in pulmonary function following thoracic operations than nonobese patients.

Cardiovascular Function

Absolute blood volume and cardiac output are increased in obesity. The presence of OSA further increases the risks of pulmonary and systemic hypertension. These factors eventually lead to "eccentric" right ventricular hypertrophy, left ventricular hypertrophy, and development of right and left heart failure ("obesity cardiomyopathy") in older MO patients [14]. A routine electrocardiogram is usually adequate for most MO patients, even those with arterial hypertension. However, even in asymptomatic obese patients, some degree of right ventricular dysfunction can be demonstrated by echocardiography. The presence of angina or other cardiac symptoms requires a more thorough cardiac evaluation. Longstanding or severe OSA should alert one to the possibility of pulmonary

hypertension and right ventricular failure and prompt preoperative echocardiographic evaluation [15].

Obstructive Sleep Apnea

Although OSA has important implications for airway management and for the perioperative use of sedatives and opiates, most MO surgical patients have not had a polysomnographic (PSG) "sleep" study to confirm the diagnosis. The anesthesiologist performing the preoperative assessment may be the first person to suspect OSA [16].

Suspicion of OSA is raised for any patient with a BMI $>35 \text{ kg/m}^2$, particularly when the adipose has an abdominal distribution ("central" obesity) with increased waist-to-hip ratio, a large neck circumference ($>17 \text{ in.}$ or $>43 \text{ cm}$ in men, $>16 \text{ in.}$ or $>40 \text{ cm}$ in women), and a Mallampati airway score of III or IV. Besides snoring, frequent awakenings and apnea periods during sleep, OSA patients often have a history of day-time drowsiness, morning headaches, irritability, personality changes, depression, cognitive impairment, and visual incoordination.

Intermittent nocturnal sympathetic activation from hypoxemia and hypercarbia causes systemic hypertension. Recurrent hypoxic pulmonary vasoconstriction eventually results in pulmonary hypertension and right and left ventricular hypertrophy. Medical comorbidities are independently associated with both obesity and OSA and include hypertension, coronary artery disease, cerebrovascular disease, congestive heart failure, cardiac dysrhythmias, and diabetes mellitus [17].

The STOP questionnaire (mnemonic for Snoring, Tiredness, Observed you stop breathing, blood Pressure) has been developed to help identify OSA patients [18, 19]. The STOP questionnaire when combined with important patient data (BMI, age, neck size, gender) has a very high sensitivity for identifying patients with moderate to severe OSA. However, a PSG study is the only accurate means of assessing the severity of OSA.

During PSG numerous parameters are recorded and then analyzed. The Arousal Index (ARI) is the number of apneas/hour of total sleep time. The Hypopnea Index (HI) is the number of hypopneas/hour of total sleep time. The sum of the ARI and HI is the Arousal/Hypopnea Index (AHI) [5]. The Arousal Index (ARI) is the number arousals/hour of total sleep. The combination of ARI and AHI is the Respiratory Disturbance Index (RDI). An AHI of >5 in combination with clinical symptoms is considered diagnostic of OSA.

Obtaining a complete preoperative PSG study, although ideal, may not be practical depending on availability of a sleep laboratory, the cost, and the urgency of surgery. Since OSA is so common in the MO population (in some studies $>80\%$), all patients should be presumed to have OSA and be managed within that context. The American Society of Anesthesiologists (ASA) consensus guideline document for the perioperative management of patients with OSA is an extremely useful

resource for planning the perioperative management of any MO patient undergoing thoracic surgery [20].

CPAP, administered by nasal mask or prongs, is used to treat moderate to severe OSA. CPAP provides a pneumatic stent that opens the upper airway and maintains its patency. For patients requiring high levels of CPAP or those with chronic obstructive pulmonary disease as occurs in many thoracic surgical patients, bi-level positive airway pressure (BIPAP) is used since it allows for independent adjustment of inspiratory and expiratory positive airway pressure unlike the fixed single setting for CPAP [21]. OSA patients scheduled for an elective procedure can experience significant improvement in their symptoms if they are begun on CPAP therapy preoperatively. Tongue volume decreases and pharyngeal space actually enlarges following several weeks of CPAP, potentially simplifying airway management. Preoperative CPAP also improves other medical comorbidities including congestive heart failure, hypertension, and perhaps even pulmonary hypertension.

Obesity Hypoventilation Syndrome

OHS patients present with the same symptoms as OSA patients, but usually have lower daytime oxygen saturations and more severe pulmonary hypertension.

Electrocardiographic evidence of right heart strain and hypertrophy is common. A preoperative arterial blood gas sample, preferably with the patient breathing room air, should be obtained. It will establish a baseline, and document the degree of PaCO_2 elevation and the presence of elevated bicarbonate levels compensating for chronic respiratory acidosis. Polycythemia is usually present secondary to chronic hypoxemia, and this further increases an already elevated risk for postoperative pulmonary embolism.

Compared with eucapnic MO patients with sleep-disordered breathing, patients with OHS have higher risk of developing serious cardiovascular disease. Given that the prevalence of extreme obesity has increased considerably, it is likely that clinicians will encounter patients with OHS who are scheduled for thoracotomy. Therefore, maintaining a high index of suspicion can lead to early recognition and treatment reducing the high morbidity and mortality associated with undiagnosed and untreated OHS [22].

Management of Anesthesia

Premedication

Centrally depressant medications can decrease ventilatory responsiveness to hypoxemia and hypercarbia in any MO patient, but in the MO patient with OSA these drugs also decrease pharyngeal dilator muscle tone and activity causing upper airway collapse. Many anesthetic agents and medications are associated with pharyngeal collapse; including

opioids, benzodiazepines, nitrous oxide, thiopental, propofol, and even small doses of neuromuscular blocking agents. Sedatives given preoperatively can have prolonged effects in any MO patient, and when OSA is present they increase the risk of respiratory depression even into the postoperative period. For MO thoracic surgical patients, sedative premedication should be used with caution or preferably, avoided completely.

Patient Position

Unlike normal-weight patients, awake MO patients should never be allowed to lie flat prior to induction of anesthesia. In the supine position, MO patients experience an exacerbated reduction in their already reduced FRC. This can result in dangerous hypoxemia, especially if they are breathing air. Obese patients preoxygenated in sitting position have significantly extended tolerance to apnea after muscle paralysis ("safe apnea time") when compared with similar patients preoxygenated in the conventional supine position [23]. Also, in the supine position any decreased venous return from compression of the inferior vena cava by increased abdominal pressure can cause hypotension.

MO patients should always be positioned prior to anesthetic induction so that their upper body and head are elevated to a point that their sternum and ear are aligned in a horizontal line (HELP) [24] (Fig. 26.1). In addition, if the patient is hemodynamically stable, the operating room table should be in the RTP [25]. The Semi-Fowler position with the patient's upper body elevated 25–30° also extends safe apnea time [26] but the 30° RTP is better [27]. In these positions the patient's



FIG. 26.1. Prior to induction of general anesthesia, the morbidly obese patient should never be allowed to lie flat but should be positioned in the head-elevated laryngoscopy position (HELP). In this position, an imaginary horizontal line can be drawn from their sternum to their ear. HELP improves the view during direct laryngoscopy and increases safe-apnea time after muscle paralysis. If the patient is hemodynamically stable, the operating table should be in 30° reverse Trendelenburg to further increase safe-apnea time.



FIG. 26.2. After turning the patient to the lateral decubitus flexed position, supporting the patient's head can be difficult due to a proportionally short neck in many MO patients. Creative placement of towels and blankets is required to ensure that the head is positioned on a horizontal line extending through the spine of the patient, in a neutral position.

pannicles drops down and “unloads” the diaphragm, which in turn increases FRC. The combination of the patient in the HELP with the operating room table in the RTP maximizes FRC and improves the view during direct laryngoscopy.

The head-up position in obese patients, without adequate arm support, can result in brachial plexus injury [28]. Changing to the lateral position for thoracotomy or thoracoscopy requires additional physical help and equipment. Axillary rolls have to be proportionally larger to protect the brachial plexus. Beanbags to support the patient in the lateral decubitus position may not sufficiently wrap around the patient due to their excessive girth and patients may need to be restrained with belts or tape across the pelvis. Supporting the head in the lateral, flexed position can be difficult due to a proportionally short neck, and requires creative placement of towels and blankets to ensure that the head is positioned on a horizontal line extending through the spine of the patient, in a neutral position (Fig. 26.2).

Anesthetic Drugs

The ASA guidelines for the perioperative management of OSA patients should be considered for all MO surgical patients, with or without a PSG diagnosis of OSA [20]. When practical, opioid-sparing anesthetic techniques including regional anesthesia should be considered. Short-acting anesthetic and analgesic agents are always appropriate choices for the MO patient. Some anesthesiologists prefer a total intravenous anesthesia (TIVA) technique with propofol and remifentanil, while most find an inhalational technique combined with epidural analgesia best for thoracotomy.

In current anesthetic practice, propofol is the induction agent of choice for surgical patients, including MO patients. In theory a lipid soluble agent like propofol should be dosed

according to TBW, but such large doses could result in cardiovascular collapse, particularly in the intravenous fluid restricted thoracotomy MO patient. For MO patients, the induction dose of propofol is based on LBW [29].

Succinylcholine should be used for tracheal intubation in the MO patient. The concentration of pseudo-cholinesterase, the enzyme that metabolizes succinylcholine, increases with increasing weight. The dose of succinylcholine (1 mg/kg TBW) provides a rapid and profound neuromuscular block and better intubating conditions [30]. Nondepolarizing muscle relaxants are initially dosed based on LBW, and a neuromuscular monitor is used to guide additional dosing.

Remifentanil is administered based on LBW in MO patients. All opioids have respiratory depressant properties and intravenous administration should be carefully titrated according to individual patient needs.

Isoflurane is more lipophilic than desflurane or sevoflurane. Desflurane and sevoflurane have each been marketed as anesthetics for MO patients. However, in obese patients blood flow to fat is reduced and comparable recovery times with both agents have been reported in obese and nonobese subjects after anesthetic procedures lasting 2–4 h. There are no clinical differences in emergence and recovery profiles in MO patients receiving either desflurane or sevoflurane when anesthetic concentration are carefully titrated [31], and despite claims to the contrary there is no clear advantage between any of the inhalational anesthetics in MO patients [32].

Tracheal Intubation

The American Society of Anesthesiologists Task Force defines a difficult airway as the “clinical situation in which a conventionally trained anesthesiologist experiences problems with (a) face mask ventilation of the upper airway or (b) tracheal intubation, or both” [33].

The criteria used to define difficult mask ventilation usually include failure to maintain oxygen saturation (SpO_2) >92%, the need for two providers, and/or the inability to mask ventilate at all. Increased BMI and a history of OSA are each independent predictors for difficult mask ventilation [34], and there is general acceptance that MO patients, especially when supine, are more difficult to ventilate by mask than normal-weight patients.

Numerous studies have considered tracheal intubation in the MO population. The view obtained during direct laryngoscopy is usually used as a measure for difficult or failed intubation; however, an ETT may be easy to place despite a poor laryngoscopic view, and even with a reasonable view there can be difficulty passing a tube.

A controversy remains as to whether the tracheas of all MO patients are more difficult to intubate than normal patients [35]. Airway studies in MO patients are often performed on the bariatric surgical population, which typically includes a greater number of female patients. Male fat deposition usually exhibits a more visceral and truncal pattern than the

peripheral deposition seen in females. Higher rates of OSA are seen in men due to a greater accumulation of fat around the airway [36]. It is therefore possible that many studies of the airway in MO select greater numbers of patients where the anatomical impact of obesity is reduced. In addition, a lack of a standard intubating position in MO patients further confuses the issue.

The standard sniffing position for tracheal intubation is achieved in nonobese patients by raising their occiput 8–10 cm with a pillow or head rest. Obese patients require much greater elevation of their head, neck, and shoulders (HELP) to produce the same alignment of axes for intubation [24]. In studies of MO patients where the head position is suboptimal, that is, not in the HELP there are higher incidences of grade 3 and 4 Cormack–Lehane laryngoscopic views and exaggerated difficulty with direct laryngoscopy [37].

Certain clinical features are more likely to be present in obese or MO patients in whom direct laryngoscopy is difficult. High Mallampati score (III or IV), increased neck circumference (>48 cm), and excessive pretracheal adipose tissue have consistently been identified as predictors of difficult laryngoscopy in MO patients [10, 38, 39]. It is likely that a small subset of male MO patients with short wide necks, OSA, and high Mallampati scores will present difficulty with laryngoscopy and intubation. Anesthesiologists should always proceed with caution with MO patients since difficult oxygenation by mask is very common and all have a shortened safe apnea time after apnea is induced for laryngoscopy.

It was previously believed that all MO patients were at risk for acid aspiration during induction of general anesthesia. Risk factors include increased intra-abdominal pressure, high incidence of gastroesophageal reflux disease (GERD) and hiatus hernia, increased gastric volume (usually >25 mL), and decreased gastric fluid pH (usually <2.5). Recently, this belief has been challenged and it now felt that most patients are at no greater risk than normal-weight patients. Obese patients at special risk for gastric acid aspiration are those with diabetes and gastroparesis, and patients who have previously undergone gastric banding procedures [40].

For most MO patients, an intravenous induction with propofol and succinylcholine is the best means for securing the airway. As short a period as possible between making the patient apneic and successful tracheal intubation is important since bag and mask ventilation is often difficult due to upper airway obstruction and reduced pulmonary compliance, and gastric insufflation during ineffective mask ventilation will increase the risk of regurgitation and acid aspiration. A second person experienced with airway management, preferably another anesthesiologist, should always be readily available to assist when difficulty is encountered.

Lung Separation

Safe and dependable isolation and selective ventilation of the lungs are essential for the practice of modern thoracic

anesthesia. Lung separation is accomplished with either a double-lumen tube (DLT) or bronchial blockade (BB) using a balloon-tipped catheter. There is no “best” method for lung separation, and choice depends on the specific surgical requirements, the patient’s airway, and the individual anesthesiologist’s preferences and experience.

To date there have been no studies comparing ease and success of DLT placement in obese patients with normal-weight patients. As discussed, direct laryngoscopy for placement of a DLT or endotracheal tube (ETT) should be no more difficult in the majority of MO patients provided the patient is appropriately positioned for laryngoscopy.

When a problematic laryngoscopy is anticipated, or if difficulty is actually experienced when attempting to place a DLT, a single lumen ETT can be inserted using a gum elastic bougie as a guide, or through any of several laryngeal mask airways (LMAs) using fiberoptic bronchoscopy, or with any other intubation adjunct such as a Trachlight® [41, 42]. Once the ETT is in place, a bronchial blocker can be used, or alternatively, a long tube exchanger can be employed to change from the ETT to a DLT. A DLT can also be placed directly by fiberoptic bronchoscopy [43].

When tube exchange is not practical, lung isolation can usually be achieved with a bronchial blocker through the ETT. BB may be the best choice for those MO patients with high Mallampati score and thick necks who present with a potential “difficult” airway. If the plans are to use an ETT for postoperative ventilation, it may be safer to avoid a DLT entirely since changing tubes at the completion of surgery can be potentially dangerous in these patients.

A major advantage for selecting a DLT for a MO patient is the ease that CPAP can be applied to the collapsed lung to improve oxygenation during OLV. Our usual practice for all patients is to select a DLT by examining the patient’s chest radiograph or CT scan preoperatively to determine tracheobronchial anatomy and airway diameters [44]. Unlike chronic obstructive lung disease, which results in a dilation of trachea and bronchi, a similar effect does not occur for the restrictive lung disease associated with obesity. Relatively, small tracheas are often found in a very large number of patients. A large lumen DLT will minimize airflow resistance and reduce intrinsic PEEP (PEEP) during OLV [45].

One-Lung Ventilation

Surgical positions affect the severity and progress of hypoxemia during OLV. Successful OLV in MO patients is technically possible in the lateral position if the panniculus is allowed to fall away from the body unloading the dependent diaphragm (Fig. 26.3). I coauthored the single published clinical series of MO patients undergoing thoracotomy almost 30 years ago. That study found that MO patients tolerated the surgical procedure with adequate oxygenation during OLV, although their arterial oxygen tensions were significantly lower during OLV than normal-weight controls [46].



FIG. 26.3. Successful one-lung ventilation (OLV) in MO patients is technically possible in the lateral position if the panniculus is allowed to fall away from the body unloading the dependent diaphragm. MO patients are much less likely to tolerate OLV in the supine position since many patients already have reduced FRC and are relatively hypoxic even during two-lung ventilation when they lie flat.

Normal-weight patients undergoing OLV in the supine position have significantly lower arterial oxygen tensions than when the same patient is in lateral position [47]. For patients undergoing thoracotomy in the supine, the semi-lateral decubitus, and the lateral decubitus positions, oxygenation progressively decreases with time after the start of OLV. However, OLV in the supine position is associated with the highest incidence of life-threatening hypoxemia, usually occurring approximately 10 min after starting OLV with 100% oxygen inhalation [48]. Although MO patients maintain adequate oxygenation during OLV in the lateral position, they are much less likely to tolerate OLV in the supine position since many patients already have reduced FRC and are relatively hypoxic even during two-lung ventilation lying flat.

MO patients benefit from lung recruitment maneuvers following induction of anesthesia, particularly prior to the institution of OLV [49]. For most patients maintaining intraoperative oxygenation during OLV can be accomplished with tidal volume ventilation of 10–12 mL/kg (IBW) or less, intermittent alveolar recruitment, CPAP to the collapsed lung, or PEEP to the ventilated lung [50]. Basilar atelectasis is present in supine MO patients preoperatively, and worsens following induction of general anesthesia. Ventilation with tidal volumes greater than 13 mL/kg (IBW) does not improve oxygenation, and can result in excessively high peak pressures during OLV [51].

High peak inspiratory pressures secondary to restriction of chest wall and diaphragmatic excursion and the narrow single lumen of a DLT can further limit volume-controlled mechanical ventilation during OLV. Pressure-controlled ventilation during

OLV can improve oxygenation and decrease peak pressures in normal-weight patients [52]. Pressure-limited OLV may have an application in the MO population, but if too low a tidal volume is delivered to a patient with an already low FRC, hypoxemia will worsen. PEEP is beneficial during two-lung ventilation in MO patients. During OLV, the benefits of PEEP to the single ventilated dependent lung are less clear as any pressure above the lower inflection point of the alveolar pressure–volume loop results in increased pulmonary vascular resistance thereby increasing shunt fraction and worsening hypoxemia [53].

Tracheal Extubation

Extubation of the trachea at the completion of a pulmonary resection lowers the risk of bronchial stump disruption and pulmonary air leaks secondary to positive pressure ventilation. In normal patients, our practice is to extubate the trachea early with the patient still in the lateral position, followed by assisted mask ventilation until the patient is fully awake. In the MO patient, especially one with a history of OSA, mask ventilation can be difficult. Tracheal extubation in a MO patient should be performed with the operating room table in the RTP to optimize ventilation and to allow access to the airway if reintubation becomes necessary.

A MO patient must be sufficiently awake and have a regular respiratory pattern before the trachea is extubated. The DLT can be replaced with an ETT via a tube exchanger and the patient is allowed to emerge from anesthesia. Alternatively, after deflating both the tracheal and bronchial cuffs and withdrawing the tube until the endobronchial segment is in the trachea, the tracheal cuff can be reinflated and the DLT used as a single lumen tube. A DLT completely in the trachea is less stimulating than one still in the bronchus.

For the MO patient who has been using CPAP or BIPAP preoperatively, these devices should be available and used immediately after tracheal extubation to stent the upper airway, to reduce the work of breathing, and to improve tidal volume and gas exchange [54]. The recently introduced non-invasive Boussignac mask-CPAP (BCPAP) system does not require a mechanical ventilator and is very helpful in maintaining satisfactory oxygenation in spontaneously breathing MO surgical patients [55, 56]. Supplemental oxygen should always be administered, but oxygen therapy can increase the AHI, hypoventilation, and PaCO_2 levels in OHS patient.

Continuous, noninvasive, transcutaneous carbon dioxide (PtCO_2) monitoring, when compared to standard arterial blood gas sampling, is accurate and has been applied to MO patients, especially those with OSA and OHS to evaluate abnormalities in their alveolar ventilation [57].

Intravenous Fluid Management

Routine clinical practice is to restrict intravenous fluid to reduce the incidence of postoperative pulmonary edema after lung resection [58]. Therefore, perioperative assessment of

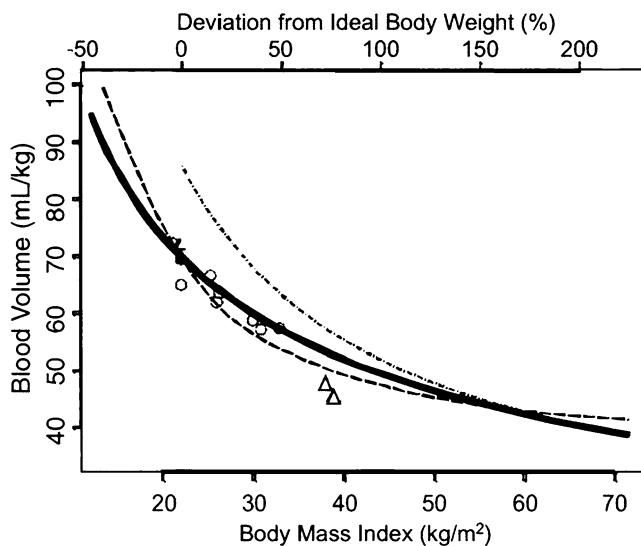


FIG. 26.4. Routine clinical practice is to restrict intravenous fluid during lung resection. The mean value for blood volume (BV) in normal-weight adults ($BMI < 25 \text{ kg/m}^2$) is approximately 70 mL/kg . BV decreases in a nonlinear manner with increasing weight. With increases in BMI total circulating BV also increases, but BV measured as mL/kg TBW decreases in a nonlinear manner. Calculating blood loss and fluid resuscitation using 70 mL/kg will overestimate BV in MO patients and can lead to under-administration of crystalloids, colloids, and red blood cells in the event of massive fluid translocation and/or hemorrhage. (Adapted from Lemmings et al. [59].)

Blood volume (BV) is particularly critical for patients undergoing thoracotomy. The mean value for BV in normal-weight adults is usually given as 70 mL/kg . Since BV decreases in a nonlinear manner with increasing weight, this value cannot be used for obese and MO patients. With progressive increase in BMI total circulating BV also increases, but BV measured as mL/kg TBW actually decreases in a nonlinear manner [59] (Fig. 26.4). Using 70 mL/kg will overestimate BV in MO patients and can lead to under-administration of crystalloids, colloids, and red blood cells in the event of massive fluid translocation and/or hemorrhage.

Postoperative Analgesia

Satisfactory postthoracotomy analgesia is extremely important to maximize lung function, particularly in the MO patient who has baseline restricted lung function prior to surgery.

Epidural opioid analgesia, with or without local anesthetic, when compared to intravenous (IV) opioids reduces pain, improves pulmonary function and oxygenation, and reduces postthoracotomy complications [60]. Local anesthetics given epidurally also supplement general anesthesia and reduce opioid needs during surgery.

Lung volumes in obese patients are probably significantly further reduced in the postoperative period. Although the effects of thoracic epidural analgesia (TEA) compared to conventional opioid-based analgesia in postoperative spirometry has not

been studied in obese patients undergoing thoracotomy, it has in laparotomy patients [13]. In both groups, perioperative spirometric values decreased significantly with increasing BMI, with the greatest reduction in vital capacity immediately after tracheal extubation. The effects were less in all patients receiving TEA, but in obese patients ($BMI > 30 \text{ kg/m}^2$) the difference in vital capacity was significantly more pronounced than in normal patients. Recovery of spirometric values was significantly quicker in patients receiving TEA, particularly in the obese patients.

With epidural analgesia, any postoperative hypotension and/or motor blockade from the local anesthetic will limit the MO patient's ability to ambulate increasing their already greater risk for pulmonary embolism.

Continuous thoracic paravertebral analgesia is as effective as epidural analgesia in managing postthoracotomy incisional pain and is associated with a lower incidence of complications, including fewer pulmonary complications, less nausea and vomiting, less hypotension, and fewer failed blocks than epidural analgesia [61]. Only the operated side is blocked.

Early institution of postoperative multimodal analgesic regimens that include local anesthetics, interpleural local anesthetic infusions, nonsteroidal anti-inflammatory agents, and other synergistic drugs to reduce the respiratory depressant effects of centrally acting agents is indicated for MO patients with OSA. Alpha-2 agonists (clonidine, dexmedetomidine) do not depress respiration and have analgesic properties. They have been used as adjuncts to epidural local anesthetics for postthoracotomy analgesia [62, 63]. Although their potential for perioperative care in MO OSA thoracic patients is promising, their role remains to be further elucidated.

Complications

Studies have reported that extremely obese patients undergoing cardiac surgical procedures have longer recovery times and a greater incidence of postoperative complications and mortality than normal-weight patients [64–66]. Although the same may be true for MO patients undergoing thoracotomy, there have been too few outcome studies to corroborate this, and most of the published postthoracotomy outcome studies have considered obese ($BMI > 30 \text{ kg/m}^2$) and not MO or super-obese patients [67, 68]. One recent study did find a weak correlation between obesity ($BMI > 30 \text{ kg/m}^2$) and increased length of hospital stay after thoracic surgery [69]. It is interesting to note that there was a much higher association of complications in low BMI ($< 18.5 \text{ kg/m}^2$) patients following thoracotomy. Many other large series of patients undergoing nonthoracic operations have reported similar results, that is, obesity ($BMI > 30 \text{ kg/m}^2$) is not a major risk factor, but low BMI ($< 18.5 \text{ kg/m}^2$) is highly associated with surgical complications and death [70].

The risk of postoperative thromboembolism, atelectasis, and pneumonia are believed to be greater in MO surgical patients undergoing nonthoracic operations [71–73]. Presumably, the

same is true for similar size patients undergoing thoracic surgery, but once again, no studies are available that can document this concern. In fact, the widely held belief of a greater incidence of complications in obese patients after nonthoracic surgery has been challenged [74].

There is one postoperative complication that is now recognized as relatively common in MO surgical patients, but rare in normal-weight patients. Rhabdomyolysis (RML) results from pressure injury to skeletal muscle due to prolonged stasis in a nonphysiologic position, such as the lateral decubitus position [75, 76]. Long-duration surgery is the major risk factor, but other factors include super-obesity, male patients, and a history of hypertension, diabetes and/or peripheral vascular disease. Intraoperative padding of all pressure points and close attention to patient positioning are essential to prevent RML, pressure ulcers, and neurologic damage in MO patients.

Injured muscle releases myoglobin, electrolytes, and protein into the systemic circulation. Myoglobinuria can lead to acute renal failure (ARF), and electrolyte disturbances can cause dysrhythmias and even cardiac arrest. Local signs and symptoms of RML are nonspecific and include pain, tenderness, swelling, bruising, and weakness. Complaints of numbness and muscular pain are almost always present, but epidural analgesia can mask symptoms and delay diagnosis.

Myoglobinuria usually presents as “tea” or brown-colored urine. The primary diagnostic indicator of RML is elevated serum creatine phosphokinase (CPK) levels. A MO patient who complains of buttock, hip, or shoulder pain in the postoperative period and who has a serum CPK level $>1,000$ IU/L is considered to have RML. Aggressive treatment should be instituted once CPK levels increase beyond 5,000 IU/L. Although intraoperative fluid replacement can reduce the risk of postoperative RML, fluid replacement is usually restricted during pulmonary resections. However, once a diagnosis of RML is made, aggressive hydration with large volumes of intravenous fluids and administration of diuretics are required to flush myoglobin from the kidneys.

Surgical Issues

Operative exposure in a MO patient may be less than optimal as the usual lateral decubitus position with extreme table flexion may not result in an adequate opening of the chest wall. Exposure is further compromised by increased chest wall thickness. Soft-tissue thickness also becomes important during video-assisted thoracoscopy (VATS) procedures since longer instruments are needed and range of motion may be limited. Unsatisfactory conditions for VATS can lead to more frequent conversion to thoracotomy, but once again, it is unclear as to whether this complication occurs more often in MO patients. The possibility of changing from VATS to open thoracotomy has important implications since it raises issues as to whether an epidural catheter should be placed

preoperatively in a “technically difficult” VATS patient when there is a high likelihood of proceeding to thoracotomy.

Conclusion

Although MO patients comprise an ever-increasing percentage of the thoracic surgical population, current anesthetic management is based on experience from obese patients undergoing nonthoracic surgical procedures. Obesity is not a contraindication to thoracic surgery, however, given the potential problems of extreme obesity there is a need for clinical studies to develop specific anesthetic management strategies for the MO thoracic surgical patient.

Clinical Case Discussion

Case: An active, working 50-year-old, 5'11" man weighing 325 lbs is scheduled for a right upper lobectomy for lung cancer confirmed by needle biopsy. The patient has no known medical problems. He has never been hospitalized and has no history of previous surgery. On questioning, his wife notes loud snoring and frequent arousals during the night, but he has never had a sleep study to diagnose OSA. The patient and surgeon are anxious to proceed with surgery as soon as possible.

Preoperative management:

What pulmonary functions studies are needed?

- Although spirometry may be useful, it is doubtful that it would demonstrate an inability for this patient to tolerate the surgery. The patient is active and has no respiratory impairment.

Should the patient undergo a preoperative PSG study?

- Given the patient's BMI (45 kg/m^2) and history of sleep disturbances, it is more than likely that he has OSA. Although PSG would confirm the diagnosis, even without it this patient should be treated as if he has OSA.

Should the surgery be postponed several weeks while the patient is placed on CPAP?

- Several weeks of preoperative CPAP therapy might be helpful, but the patient is anxious to proceed with the surgery immediately.

Intraoperative management:

What needs to be done prior to induction of anesthesia?

- In the preoperative area even if the patient is anxious, he should not be given any sedatives.
- An epidural should be placed for intra and postoperative use. It is even more important for this patient not to rely on an opioid PCA for postoperative analgesia.
- An arterial line should be placed to obtain a baseline blood gas, and for intra and postoperative monitoring.

- On arrival in the operating room, he should not be allowed to lie flat. He should be immediately positioned on the operating table in the HELP.

How should the patient's airway be intubated?

- If the preoperative assessment demonstrated a high Mallampati score and large neck circumference, a potentially difficult airway intubation is likely. The choice of proceeding with an "awake" fiberoptic intubation or a conventional IV induction and direct laryngoscopy is up to the confidence and experience of the anesthesiologist. A second trained physician or nurse should be immediately available to assist with mask ventilation and/or airway intubation.
- Whichever method is chosen, the patient should be preoxygenated for 3–5 min with 100% oxygen. If an IV induction is chosen, propofol and succinylcholine should be used. If with direct laryngoscopy the patient has a Cormack–Lehane grade \geq II view, a gum elastic bougie should be inserted through the glottis, followed by an endotracheal tube (ETT) over the bougie. At this point lung separation can then be accomplished with either a bronchial blocker through the ETT, or the ETT can be replaced with a DLT using an 80 cm DLT-exchange catheter. If intubation by direct laryngoscopy and a bougie is not possible, an LMA should be placed and a fiberoptic bronchoscope used to intubate the trachea with an ETT.

Postoperative management:

What if the patient complains of pain, even with a functioning epidural?

- Supplemental IV opioid analgesia should be avoided; multimodal analgesic techniques should be considered.
- In the postoperative area the patient is noted to be oliguric?
- The differential diagnosis includes hypovolemia and the need to administer IV fluids.
- A serum CPK level should be obtained to rule out renal failure secondary to rhabdomyolysis. If the CPK level is $>1,000$ IU/L, aggressive fluid therapy should be instituted.

References

1. Lohser J, Kulkarni V, Brodsky JB. Anesthesia for thoracic surgery in morbidly obese patients. *Curr Opin Anesthesiol*. 2007;20:10–4.
2. Baskin ML, Ard J, Franklin F, et al. Prevalence of obesity in the United States. *Obes Rev*. 2005;6:5–7.
3. Lemmens HJ, Brodsky JB, Bernstein DP. Estimating ideal body weight – a new formula. *Obes Surg*. 2005;15:1082–3.
4. Davis G, Patel JA, Gagne DJ. Pulmonary considerations in obesity and the bariatric surgical patient. *Med Clin N Am*. 2007;91:433–42.
5. Stierer T, Punjabi NM. Demographics and diagnosis of obstructive sleep apnea. *Anesthesiol Clin N Am*. 2005;23:405–20.
6. Koenig SM. Pulmonary complications of obesity. *Am J Med Sci*. 2001;321:249–79.
7. Crummy F, Piper AJ, Naughton MT. Obesity and the lung: 2 Obesity and sleep-disordered breathing. *Thorax*. 2008;63:738–46.
8. Mokhlesi B, Tulaimat A. Recent Advances in obesity hypoventilation syndrome. *Chest*. 2007;132:1322–36.
9. Schumann R, Jones SB, Ortiz VE, et al. Best practice recommendations for anesthetic perioperative care and pain management in weight loss surgery. *Obes Res*. 2005;13:254–66.
10. Brodsky JB, Lemmens HJ, Brock-Utne JG, et al. Morbid obesity and tracheal intubation. *Anesth Analg*. 2002;94:732–6.
11. Pelosi P, Croci M, Ravagnan I, et al. The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. *Anesth Analg*. 1998;87:654–60.
12. Licker MJ, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg*. 2006;81:1830–7.
13. von Ungern-Sternberg BS, Regli A, et al. Effect of obesity and thoracic epidural analgesia on perioperative spirometry. *Br J Anaesth*. 2005;94:121–7.
14. Alpert MA, Fraley MA, Bircham JA, et al. Management of obesity cardiomyopathy. *Expert Rev Cardiovasc Ther*. 2005;3:225–30.
15. Sidana J, Aronow WS, Ravipati G, et al. Prevalence of moderate or severe left ventricular diastolic dysfunction in obese persons with obstructive sleep apnea. *Cardiology*. 2005;104:107–9.
16. Kaw R, Michota F, Jaffer A, et al. Unrecognized sleep apnea in the surgical patient: implications for the perioperative setting. *Chest*. 2006;129:198–205.
17. Pashayan AG, Passannante AN, Rock P. Pathophysiology of obstructive sleep apnea. *Anesthesiol Clin N Am*. 2005;23:431–43.
18. Chung F, Yegneswaran B, Liao P, et al. Validation of the Berlin questionnaire and the American Society of Anesthesiologists checklist as screening tools for obstructive sleep apnea in surgical patients. *Anesthesiology*. 2008;108:822–30.
19. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology*. 2008;108:812–21.
20. Gross JB, Bachenberg KL, Benumof JL, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea. *Anesthesiology*. 2006;104:1081–93.
21. Couch EM, Senior B. Nonsurgical and surgical treatments for sleep apnea. *Anesthesiol Clin N Am*. 2005;23:525–34.
22. Mokhlesi B, Kryger MH, Grunstein RR. Assessment and management of patients with obesity hypoventilation syndrome. *Proc Am Thorac Soc*. 2008;5:218–25.
23. Altermatt FR, Muñoz HR, Delfino AE, et al. Pre-oxygenation in the obese patient: effects of position on tolerance to apnoea. *Br J Anaesth*. 2005;95:706–9.
24. Collins JS, Lemmens HJ, Brodsky JB, et al. Laryngoscopy and morbid obesity: a comparison of the "sniff" and "ramped" positions. *Obes Surg*. 2004;14:1171–5.
25. Perilli V. Determinants of improvement in oxygenation consequent to reverse Tredelenburg position in anesthetized morbidly obese patients. *Obes Surg*. 2004;14:866–7.
26. Dixon BJ, Dixon JB, Carden JR, et al. Preoxygenation is more effective in the 25 degrees head-up position than in the supine position in severely obese patients: a randomized controlled study. *Anesthesiology*. 2005;102:1110–5.
27. Boyce JR, Ness T, Castroman P, et al. A preliminary study of the optimal anesthesia positioning for the morbidly obese patient. *Obes Surg*. 2003;13:4–9.
28. Brunette KE, Hutchinson DO, Ismail H. Bilateral brachial plexopathy following laparoscopic bariatric surgery. *Anaesth Intensive Care*. 2005;33:812–5.

29. Ingrande J, Brodsky JB, Lemmens HJM. Weight-based dosing scales for the anesthetic induction dose of propofol in morbidly obese subjects. *Anesth Analg*. 2010 Sept 22 [Epub ahead of publication]
30. Lemmens HJ, Brodsky JB. The dose of succinylcholine in morbid obesity. *Anesth Analg*. 2006;102:438–42.
31. Arain SR, Barth CD, Shankar H, et al. Choice of volatile anesthetic for the morbidly obese patient: sevoflurane or desflurane. *J Clin Anesth*. 2005;17:413–9.
32. Brodsky JB, Lemmens HJ, Saidman LJ. Obesity, surgery, and inhalation anesthetics – is there a “drug of choice”? *Obes Surg*. 2006;16:734.
33. Practice guidelines for management of the difficult airway. an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2003;98:1269–77.
34. Kheterpal S, Han R, Tremper KK, et al. Incidence and predictors of difficult and impossible mask ventilation. *Anesthesiology*. 2006;105:885–91.
35. Collins JS, Lemmens HJ, Brodsky JB. Obesity and difficult intubation: where is the evidence? *Anesthesiology*. 2006;104:617.
36. Benumof JL. Obesity, sleep apnea, the airway and anesthesia. *Curr Opin Anaesthesiol*. 2004;17:21–30.
37. Keller C, Brimacombe J, Kleinsasser A, et al. The Laryngeal Mask Airway ProSeal™ as a temporary ventilatory device in grossly and morbidly obese patients before laryngoscope-guided tracheal intubation. *Anesth Analg*. 2002;94:737–40.
38. Ezri T, Gewurtz G, Sessler DI, et al. Prediction of difficult laryngoscopy in obese patients by ultrasound quantification of anterior neck soft tissue. *Anesthesia*. 2003;58:1111–4.
39. Gonzalez H, Minville V, Delanoue K, et al. The importance of increased neck circumference to intubation difficulties in obese patients. *Anesth Analg*. 2008;106:1132–6.
40. Jean J, Compère V, Fourdrinier V, et al. The risk of pulmonary aspiration in patients after weight loss due to bariatric surgery. *Anesth Analg*. 2008;107:1257–9.
41. Combes X, Sauvat S, Leroux B, et al. Intubating laryngeal mask airway in morbidly obese and lean patients: a comparative study. *Anesthesiology*. 2005;102:1106–9.
42. Dhonneur G, Ndoko SK, Yavchitz A, et al. Tracheal intubation of morbidly obese patients: LMA CTrach vs direct laryngoscopy. *Br J Anaesth*. 2006;97:742–5.
43. Shulman MS, Brodsky JB, Levesque PR. Fibreoptic bronchoscopy for tracheal and endobronchial intubation with a double-lumen tube. *Can J Anaesth*. 1987;34:172–3.
44. Brodsky JB, Lemmens HJ. Tracheal width and left double-lumen tube size: a formula to estimate left-bronchial width. *J Clin Anesth*. 2005;17:267–70.
45. Slinger PD, Lesiuk L. Flow resistances of disposable double-lumen, single-lumen, and Univent tubes. *J Cardiothorac Vasc Anesth*. 1998;12:142–4.
46. Brodsky JB, Wyner J, Ehrenwerth J, et al. One-lung anesthesia in morbidly obese patients. *Anesthesiology*. 1982;57:132–4.
47. Bardoczky GI, Szegedi LL, d'Hollander AA, et al. Two-lung and one-lung ventilation in patients with chronic obstructive pulmonary disease: the effects of position and F(IO)2. *Anesth Analg*. 2000;90:35–41.
48. Watanabe S, Noguchi E, Yamada S, et al. Sequential changes of arterial oxygen tension in the supine position during one-lung ventilation. *Anesth Analg*. 2000;90:28–34.
49. Henzler D, Rossaint R, Kuhlen R. Is there a need for a recruiting strategy in morbidly obese patients undergoing laparoscopic surgery? *Anesth Analg*. 2004;98:268.
50. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin*. 2008;26:241–72.
51. Bardoczky GI, Yernault JC, Houben JJ, et al. Large tidal volume ventilation does not improve oxygenation in morbidly obese patients during anesthesia. *Anesth Analg*. 1995;81:385–8.
52. Senturk NM, Dilek A, Camci E, et al. Effects of positive end-expiratory pressure on ventilatory and oxygenation parameters during pressure-controlled one-lung ventilation. *J Cardiothorac Vasc Anesth*. 2005;19:71–5.
53. Michelet P, Roch A, Brousse D, et al. Effects of PEEP on oxygenation and respiratory mechanics during one-lung ventilation. *Br J Anesth*. 2005;95:267–73.
54. Frey WC, Pilcher J. Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. *Obes Surg*. 2003;13:676–83.
55. Gaszynski T, Tokarz A, Piotrowski D, et al. Boussignac CPAP in the postoperative period in morbidly obese patients. *Obes Surg*. 2007;17:452–6.
56. Neligan PJ, Malhotra G, Fraser M, et al. Continuous positive airway pressure via the Boussignac system immediately after extubation improves lung function in morbidly obese patients with obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesthesiology*. 2009;110:878–84.
57. Maniscalco M, Zedda A, Faraone S, et al. Evaluation of a transcutaneous carbon dioxide monitor in severe obesity. *Intensive Care Med*. 2008;34:1340–4.
58. Slinger PD. Perioperative fluid management for thoracic surgery: the puzzle of postpneumonectomy pulmonary edema. *J Cardiothorac Vasc Anesth*. 1995;9:442–51.
59. Lemmens HJ, Bernstein DP, Brodsky JB. Estimating blood volume in obese and morbidly obese patients. *Obes Surg*. 2006;16:773–6.
60. Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids. A meta-analysis. *Anesthesiology*. 2005;103:1079–88.
61. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy – a systematic review and meta-analysis of randomized trials. *Br J Anaesth*. 2006;96:418–26.
62. Wahlander S, Frumento RJ, Wagener G, et al. A prospective, double-blind, randomized, placebo-controlled study of dexmedetomidine as an adjunct to epidural analgesia after thoracic surgery. *J Cardiothorac Vasc Anesth*. 2005;19:630–5.
63. Hofer RE, Sprung J, Sarr MG, et al. Anesthesia for a patient with morbid obesity using dexmedetomidine without narcotics. *Can J Anaesth*. 2005;52:176–80.
64. Wigfield CH, Lindsey JD, Munoz A, et al. Is extreme obesity a risk factor for cardiac surgery? An analysis of patients with a BMI > or = 40. *Eur J Cardiothorac Surg*. 2006;9:34–40.
65. Wagner BD, Grunwald GK, Rumsfeld JS, et al. Relationship of body mass index with outcomes after coronary artery bypass graft surgery. *Ann Thorac Surg*. 2007;84:10–6.
66. Tyson 3rd GH, Rodriguez E, Elci OC, et al. Cardiac procedures in patients with a body mass index exceeding 45: outcomes and long-term results. *Ann Thorac Surg*. 2007;84:3–9.

67. Smith PW, Wang H, Gazoni LM, et al. Obesity does not increase complications after anatomic resection for non-small cell lung cancer. *Ann Thorac Surg.* 2007;84:1098–105.
68. Chataigner O, Fadel E, Yildizeli B, et al. Factors affecting early and long-term outcomes after completion pneumonectomy. *Eur J Cardiothorac Surg.* 2008;33:837–43.
69. Suemitsu R, Sakoguchi T, Morikawa K, et al. Effect of body mass index on perioperative complications in thoracic surgery. *Asian Cardiovasc Thorac Ann.* 2008;16:463–7.
70. Mullen JT, Davenport DL, Hutter MM, et al. Impact of body mass index on perioperative outcomes in patients undergoing major intra-abdominal cancer surgery. *Ann Surg Oncol.* 2008;15:2164–72.
71. Eichenberger A, Proietti S, Wicky S, et al. Morbid obesity and postoperative pulmonary atelectasis: an underestimated problem. *Anesth Analg.* 2002;95:1788–92.
72. Flier S, Knape JT. How to inform a morbidly obese patient on the specific risk to develop postoperative pulmonary complications using evidence-based methodology. *Eur J Anaesthesiol.* 2006;2:154–9.
73. Davenport DL, Xenos ES, Hosokawa P, et al. The influence of body mass index obesity status on vascular surgery 30-day morbidity and mortality. *J Vasc Surg.* 2009;49:140–7.
74. Dindo D, Muller MK, Weber M, et al. Obesity in general elective surgery. *Lancet.* 2003;361:2032–5.
75. de Menezes Ettlinger JE, dos Santos Filho PV, Azaro E, Melo CA, et al. Prevention of rhabdomyolysis in bariatric surgery. *Obes Surg.* 2005;15:874–9.
76. Kong SS, Ho ST, Huang GS, et al. Rhabdomyolysis after a long-term thoracic surgery in right decubitus position. *Acta Anaesthesiol Sin.* 2000;38:223–8.

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Key Points

- Surgery for benign chest wall deformities is most commonly performed for cosmetic reasons, but in some cases for restrictive respiratory or cardiac symptoms.
- Postexcision, chest wall defects larger than 5 cm will require reconstruction to diminish paradoxical motion and impaired gas exchange.
- All full-thickness diaphragm defects should be repaired when diagnosed to prevent late onset of perforation or strangulation of abdominal contents in the chest.
- Diaphragm eventration requires repair only for symptoms of impaired gas exchange.

Chest Wall Surgery

Tumors

Benign tumors of the chest wall include chondromas, osteochondromas, fibrous dysplasia, and desmoid tumors. Because it is often not possible at the time of surgery to be certain of the pathology, benign tumors are treated the same as malignant tumors with wide excisions. Malignant tumors of the chest wall include soft tissue sarcomas, chondrosarcomas, and other varieties of sarcoma. They are excised with wide margins of at least 4 cm including several partial ribs above and below for rib lesions. For sternal lesions, a sternotomy with corresponding resection of bilateral adjacent costal arches is performed.

Defects of the chest wall less than 5 cm are usually closed primarily and not reconstructed. Defects larger than 5 cm in any diameter are reconstructed with a synthetic mesh. Soft tissue reconstruction of larger defects may include a flap of latissimus dorsi, pectoralis major, rectus abdominus, or other muscle and/or omentum [1].

Anesthetic considerations for excision of chest wall tumors include possible invasive or compressive effects of the tumor on intrathoracic cardiovascular or respiratory structures (see Fig. 27.1). Postoperative pain and respiratory limitation is a major problem following excision of large chest wall tumors. Thoracic epidural analgesia may be indicated for patients with borderline preoperative respiratory function.

Congenital Deformities

The commonest congenital deformity of the chest wall presenting for surgery is pectus excavatum (see Fig. 27.2). This is a posterior angulation of the lower sternum and adjacent ribs. The severity can be assessed on chest imaging by the “pectus index” which is the distance ratio of the transverse chest diameter to the shortest distance between the posterior sternum and the anterior border of the spine. In normal individuals this ratio is approximately 2.5 and in patients with pectus excavatum it typically exceeds 3.5. It may be associated with scoliosis or Marfan’s syndrome. Pulmonary function tests generally show a mild restrictive pattern, however this does not improve significantly after repair [2]. However, repair of the deformity does improve exercise capacity secondary to improved cardiac output and stroke volume.

There are several different surgical procedures used to correct pectus excavatum. Most open procedures involve resection of the costal cartilages at the site of the deformity, an osteotomy of the sternum and internal fixation or stabilization (see Fig. 27.3). In children and younger adolescents, there is the option of a minimally invasive procedure with the insertion of a Nuss bar to elevate the sternum [3].

A variety of other less common congenital chest deformities such as pectus carinatum and Poland syndrome also can present for surgery. Anesthetic considerations for pectus excavatum and these other deformities are essentially identical to those for excision of chest wall tumors.

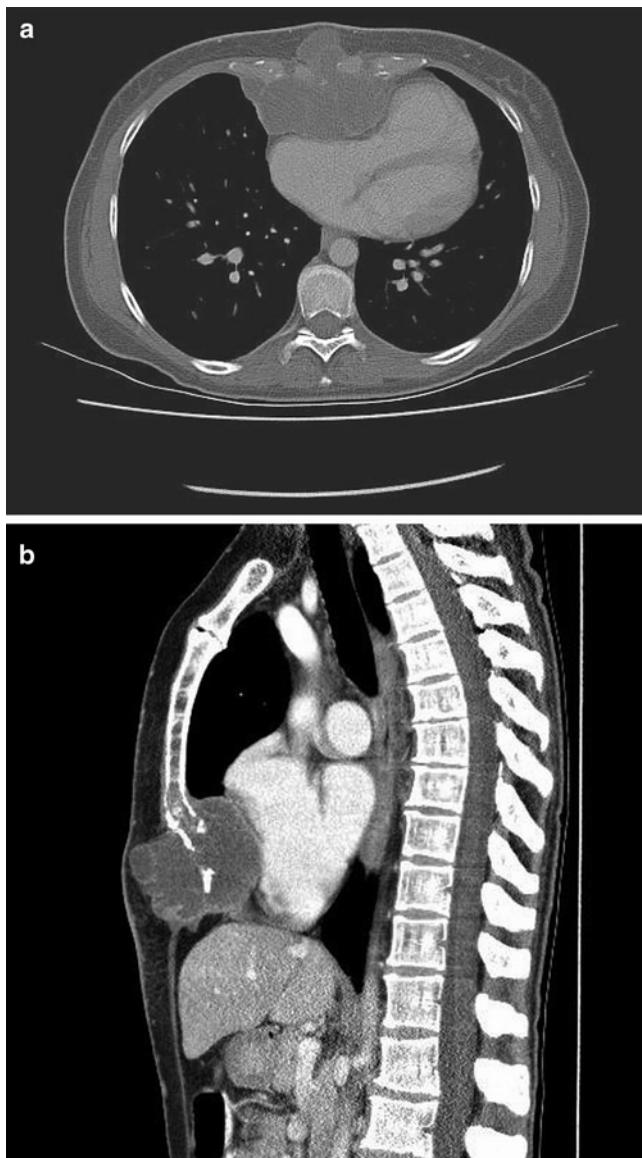


FIG. 27.1. Transverse (a) and saggital (b) CT scan views of a patient with a chondrosarcoma of the lower sternum. The tumor is compressing the right ventricle.

Thoracic Outlet Syndrome

Thoracic outlet syndrome refers to compression of the subclavian vessels and/or brachial plexus at the superior aperture of the chest. It may or may not be associated with the presence of a cervical rib. The compression is mainly caused by the first rib. Patients present with a variety of peripheral neurological or vascular symptoms which may include positional pain and paresthesia, commonly in the C8-T1 distributions of the medial hand and arm. Confirmation of the diagnosis may require nerve-conduction studies or angiography. Treatment is initially conservative with physiotherapy. In refractory cases excision

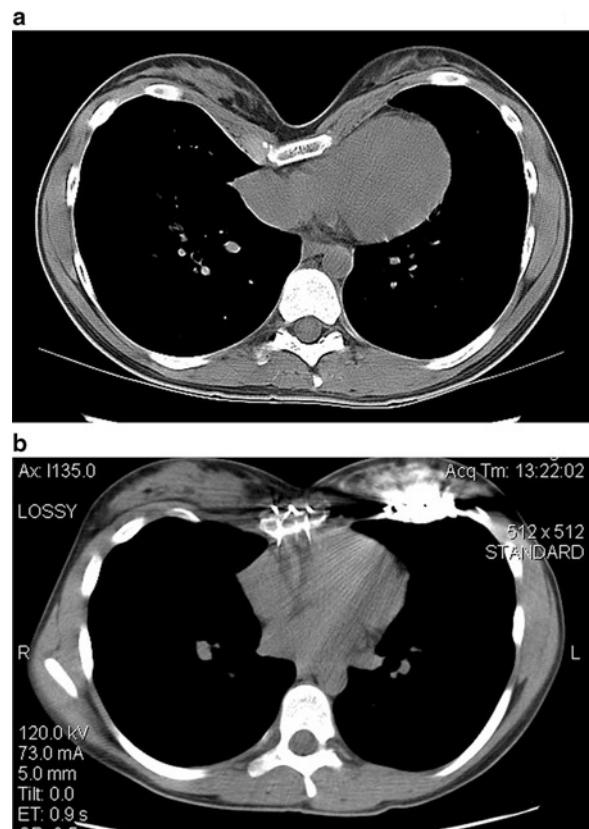


FIG. 27.2. Transverse CT scans of a patient with pectus excavatum. (a) Preoperative. The sternum is compressing the right ventricle. (b) Postoperative. Internal fixation of the sternum and a portion of the pectus bar attached to the ribs of the left chest can be seen.

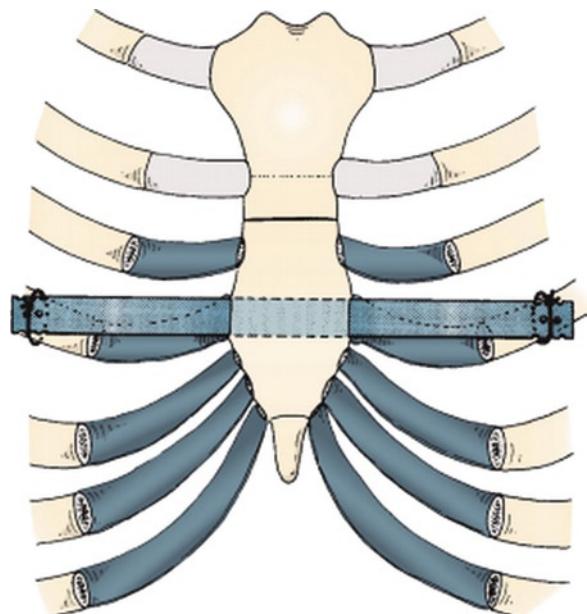


FIG. 27.3. Diagram of a pectus bar placed posterior to the lower portion of the sternum during open surgery for repair of pectus excavatum (reprinted from [5]. © Elsevier 2008, with permission).

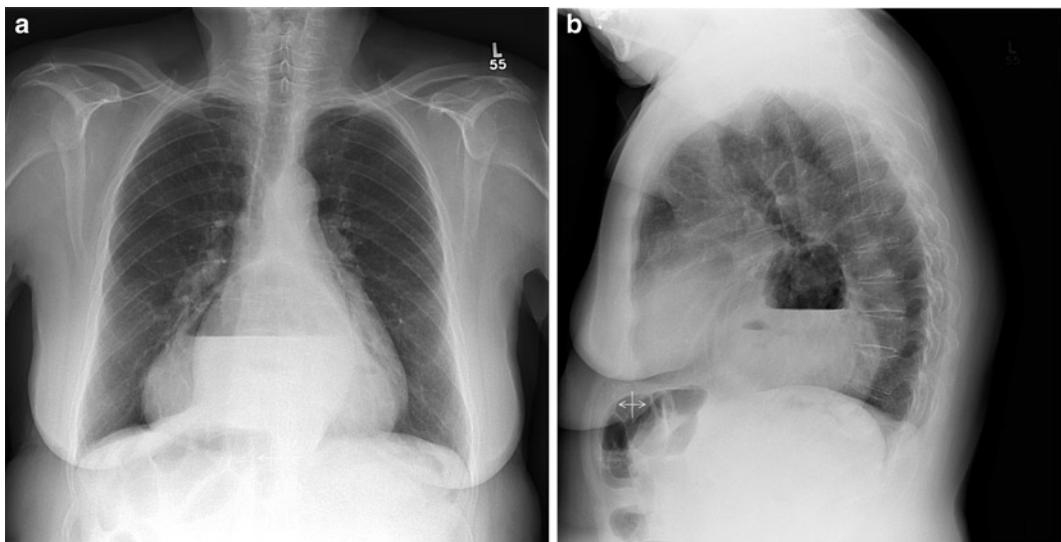


FIG. 27.4. (a) PA and (b) lateral chest X-rays of a patient with an intrathoracic stomach which has herniated through the esophageal hiatus of the diaphragm. The risk of aspiration of gastric contents during induction of anesthesia can be appreciated.

of the first rib and/or a cervical rib may be indicated. Surgery is via an extra-thoracic approach and anesthetic concerns are similar to those for other types of head and neck procedures.

Diaphragm Surgery

Hernia

Repair of congenital diaphragmatic hernia in infants is discussed in Chap. 39. Adults may also present for repair of congenital or acquired defects of the diaphragm (see Fig. 27.4). Congenital malformations of the diaphragm in adults may be diagnosed incidentally on chest imaging or may cause a variety of compressive symptoms due to the intrathoracic mass of gastrointestinal contents. The commonest site for herniation of abdominal contents into the chest is through the esophageal hiatus. Other sites include the Bochdalek foramen and Morgagni foramen. An acquired hernia may be due to sudden severe blunt abdominal trauma. Occasionally these may present late, long after the initial trauma. All diaphragmatic hernias should be repaired when diagnosed due to the possibility of strangulation or perforation of bowel in the chest. Repairs are most commonly performed by laparotomy or laparoscopy. Anesthetic concerns for hiatal hernias are similar to those for other types of benign esophageal disease (see Chap. 30) specifically, an increased risk of aspiration on induction.

Eventration

Eventration of the diaphragm is an elevation of a portion of the diaphragm due to an incomplete development of part of the musculature. The differential diagnosis is a paralysis of the diaphragm. Causes of phrenic nerve paralysis such as lung cancer must be ruled out. Most cases of eventration in adult life are treated conservatively. Severe dyspnea or orthopnea may be an indication for surgery. Surgical repair is by plication of the involved portion of the diaphragm, this can be performed with a minimally invasive approach [4].

References

1. Pairolo PC, Arnold PG. Chest wall tumors: experience with 100 consecutive patients. *J Thorac Cardiovasc Surg*. 1985;90:367–73.
2. Morshuis W, Folgering H, Barentsz J, et al. Pulmonary function before surgery for pectus excavatum and at long-term follow-up. *Chest*. 1994;105:1646–52.
3. Park HJ, Lee SY, Lee CS, et al. The Nuss procedure for pectus excavatum. *Ann Thorac Surg*. 2004;77:289–95.
4. Hutt T, Wichmann MW, Reichart B, et al. Laparoscopic diaphragmatic plication. *Surg Endosc*. 2004;18:547–51.
5. Kucharczuk J. Surgery of pectus deformities. In: Patterson GA, editor. Pearson's thoracic and esophageal surgery. 3rd ed. Amsterdam: Elsevier; p. 1333.

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Key Points

- Extrapleural pneumonectomy (EPP) is a formidable surgical procedure performed on patients with limited life expectancy. Anesthetic management may contribute to containment of perioperative morbidity and mortality through the control of intraoperative physiologic disruptions and postoperative pain, and an appreciation of the associated postoperative complications to effect early intervention.
- Beyond standard anesthetic management issues for pneumonectomy, there exist a number of important “EPP-specific” anesthetic concerns. These include significantly greater blood loss, more delicate management of intravascular fluid and blood components, greater operative impairment of venous return, high probability of arrhythmias and greater potential for hemodynamic instability related to pericardial window and its patch.
- Common causes of hypotension during EPP include compression of the heart or great vessels by tumor or surgical pressure/retraction, blood loss and/or inadequate fluid resuscitation and thoracic epidural sympathetic blockade.
- No single anesthetic recipe is of proven superiority for either EPP or lung resection surgery in general. The priority for early extubation favors the use of short-acting modern

inhalational and intravenous agents, with limited use of traditional parenteral narcotics. Thoracic epidural analgesia is widely employed intraoperatively to facilitate extubation at the conclusion of surgery by providing dense analgesia without depression of sensorium or respiratory drive.

- Fluid management remains a challenge due to the increased blood loss in EPP, hemodynamic instability, renal toxicity of chemotherapy agents, and the potential for exacerbation of acute lung injury.

Introduction

Extrapleural pneumonectomy (EPP), first described for the treatment of tuberculous empyema, is currently typically performed for local control of malignant pleural mesothelioma (MPM). Rarely, it may be applied to other malignancies or infections involving or obliterating the pleural space. The en bloc resection of lung, pleura, pericardium, and diaphragm is a formidable surgical procedure performed on patients with limited life expectancy. Although there has been a dramatic reduction in perioperative mortality from 31% reported in the 1970s [1] to recent series demonstrating mortality ranging from 3 to 7% [2–9], postoperative morbidity remains high.

Nevertheless, significant survival improvement (in selective patients with MPM) has been achieved by EPP followed by chemotherapy and/or radiation when performed at centers experienced in the procedure [2, 3, 7]. In addition, intraoperative intracavitary hyperthermic chemotherapy (IOHC) is being applied in a few centers for better control of local disease. This chapter will discuss the important “EPP-specific” anesthesia concerns [10, 11], including IOHC, which appreciably impacts on anesthetic care [11].

Malignant Pleural Mesothelioma

MPM arises on the pleural surface of the chest wall, lung, pericardium, or diaphragm, tends to spread or recur locoregionally, and is generally fatal within a year of diagnosis [12]. Its etiologic link to asbestos exposure has been established [13], but not all patients with mesothelioma have a history of asbestos exposure, and other etiologies have been postulated [14]. The current US incidence of 2–3,000 new cases/year is expected to continue to increase until at least 2020 because of the long latency period between asbestos exposure and diagnosis.

No single modality of treatment significantly improves median survival beyond 12 months. EPP offers the most complete cytoreduction, but recurrence occurs locoregionally. Multimodality approaches, combining cytoreduction by pleurectomy/decortication (P/D) or EPP, with chemotherapy, radiotherapy, or photodynamic therapy have been evaluated in various combinations recently, with reported improved survival statistics [15]. Preoperative chemotherapy followed by surgery is becoming more popular [4, 8, 9]. With the exception of IOHC, they generally do not greatly impact anesthetic management of EPP.

Intraoperative Intracavitary Heated Chemotherapy (IOHC)

The intraoperative application of chemotherapy (usually cisplatin) to address microscopic disease remaining in the empty hemithorax prior to closure is an emerging therapy with important implications on anesthetic management. Intracavitary application targets the chemotherapy directly at the sites of recurrence (including abdomen), with higher doses than would be tolerated systemically. Heating the chemotherapy agent increases tumoricidal activity by increasing the permeability and metabolic activity of the cells [16].

Surgical Considerations

Technique of EPP

The *technique of EPP* [17] consists of several basic steps:

1. Incision and exposure of the parietal pleura.

An extended posterolateral thoracotomy with resection of the sixth rib is the most common approach.

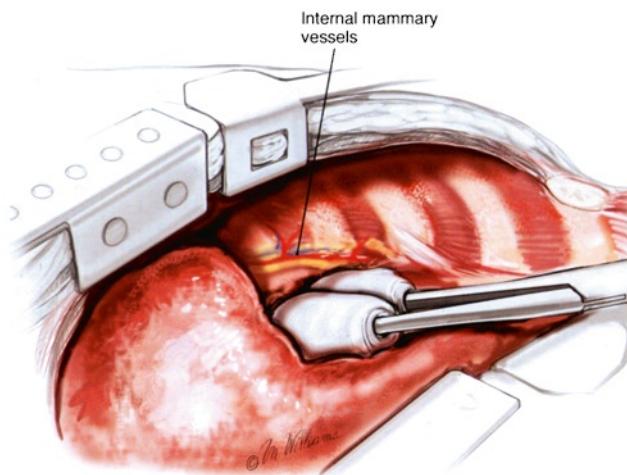


FIG. 28.1. Anterior parietal dissection (reprinted with permission from Lee et al. [17], © 2009).

2. Extrapleural dissection to separate the tumor from the chest wall.
3. En bloc resection of the lung, pleura, pericardium, and diaphragm with division of the hilar structures.

A combination of blunt and sharp extrapleural dissection is initiated anterolaterally, and advanced to and over the apex, to bring the tumor down from the posterior and superior mediastinum (Fig. 28.1).

- Beware of injury to the internal mammary vessels/grafts and subclavian vessels during dissection anteriorly and at the apex, respectively, as well as traction injury to the azygous vein and superior vena cava in the superior mediastinum.

Posterior dissection is then performed and the esophagus dissected away from the tumor. The diaphragm is avulsed circumferentially (Fig. 28.2) and the pericardium is opened.

- During division of the medial aspect of the diaphragm, the inferior vena cava may be injured or torsed.

The main pulmonary artery (PA) and pulmonary veins are then dissected, isolated, and stapled extra- or intrapericardially. After the main bronchus is dissected as far as the carina, the bronchial stapler is fired under direct visualization with the fiberoptic videobronchoscope to assure a short bronchial stump. Bleeding from numerous exposed vessels on the inner thoracic cavity is temporized by packing, but definitive hemostasis is not sought until the specimen is removed.

4. Radical lymph node dissection.

Radical mediastinal lymph node dissection is performed, followed by reinforcement of the bronchial stump. The hemithorax is then irrigated with warm saline and water (wash phase) to remove and osmotically lyse residual microscopic tumor.

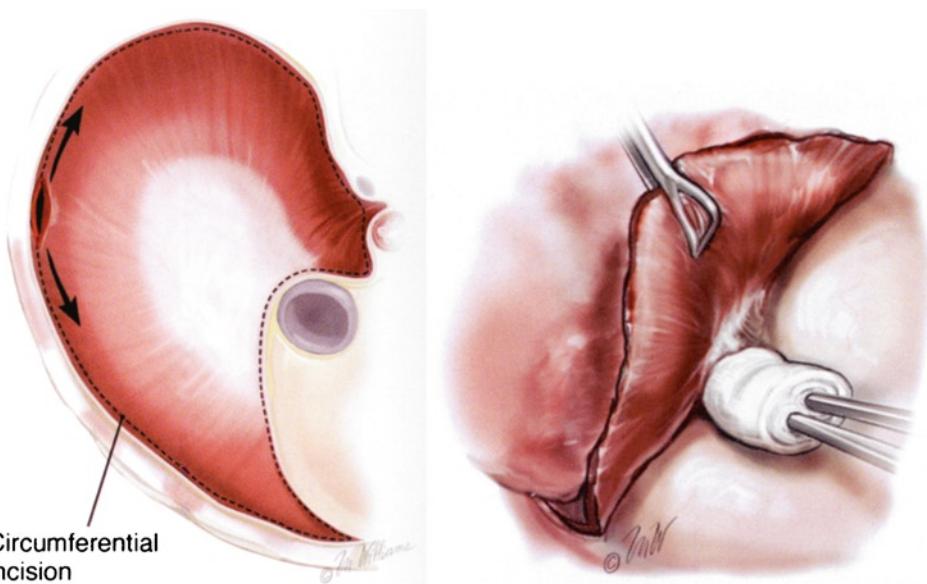


FIG. 28.2. The diaphragm is incised circumferentially and dissected bluntly from the underlying peritoneum (reprinted with permission from Lee et al. [17], © 2009).

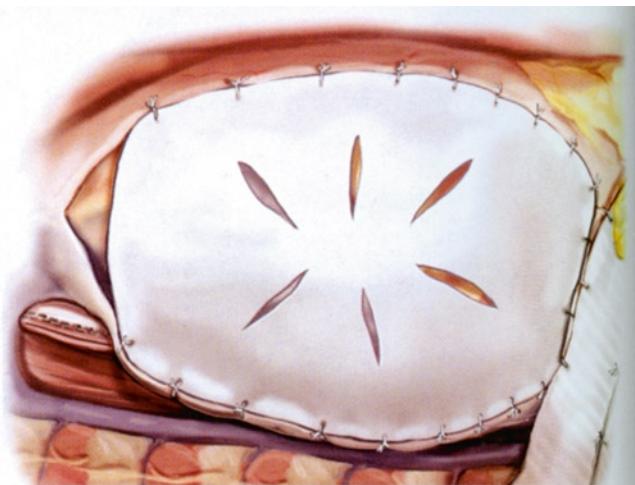


FIG. 28.3. The diaphragmatic and fenestrated pericardial patches prevent herniation (reprinted with permission from Lee et al. [17], © 2009).

5. Optional administration of IOHC.
6. Reconstruction of the diaphragm and pericardium (Fig. 28.3).

The last step is reconstruction of the diaphragm and pericardium using a prosthetic such as Gore-Tex DualMesh (W.L. Gore and Associated, Inc., Flagstaff, Arizona). These patches prevent subsequent herniation of abdominal contents and cardiac herniation into the empty hemithorax.

Technique of IOHC

Two perfusion cannulae (inflow and outflow) are placed within the open hemithorax after tumor resection and hemostasis. Chemotherapy in dialysate maintained at 42°C is circulated

TABLE 28.1. Renal protective strategies for EPP with intraoperative intracavitary hyperthermic chemotherapy (IOHC) with cisplatin (Brigham and Women's Hospital Protocol).

Admission day before surgery for intravenous hydration
Seven-day hold of nonsteroidal anti-inflammatory drugs
Pretreatment with intravenous amifostine (30 min prior to IOHC) and second dose 2 h later
Intravenous sodium thiosulfate following IOHC
Liberalized IV hydration and assiduous avoidance of systemic hypotension during and after IOHC
Urine alkalinization

via a pump for 60 min. The volume of perfusate is adjusted to keep the hemithorax full, which maximizes surface area contact between residual microscopic tumor cells and a high local concentration of cisplatin. Systemic administration of cytoprotectants is performed either before or after the chemotherapy administration depending on the agent used (Table 28.1); the timing is important to maximize tumorigenicity while sparing renal function [3]. Sodium thiosulfate covalently binds and inactivates cisplatin in the blood. Amifostine (Ethylol, Alza Pharmaceuticals – US), which exhibits 100-fold preferential uptake by normal cells and salvages intracellular free radicals, has also been used. Amifostine may cause hypotension with rapid administration.

Patient Selection

Critical to risk reduction, a general exclusion criteria utilized by the surgical group with the most favorable published survival statistics [2] are listed in Table 28.2. Patients with a predicted postoperative forced expiratory volume in 1 s (ppoFEV₁) of less than 0.8 L are considered for P/D, rather than EPP.

TABLE 28.2. Suggested exclusion criteria for EPP.

Karnovsky performance status <70%
Abnormal creatinine
Abnormal liver function tests
Evidence of unresectability by CT, MRI, echocardiogram
Room air PaCO_2 >45 mmHg
Room air PaO_2 <65 mmHg
Left ventricular ejection fraction <45%
Predicted postoperative FEV_1 <1 L ^a

^aPatients with predicted postoperative FEV_1 <2 L are recommended to undergo quantitative radionuclide ventilation-perfusion scanning
CT computed tomography; MRI magnetic resonance imaging; FEV_1 forced expiratory volume in 1 s

Preoperative Patient Preparation

An awareness of the perceived cardiopulmonary reserve, the anatomical extent and impact of the tumor, and coexisting disease states allows the anesthesiologist to tailor invasive monitors, lines, and anesthetic plan to preempt or efficiently respond to problems. If IOHC is planned, renal protection strategies begin preoperatively with hydration and the withholding of nonsteroidal anti-inflammatory medications (Table 28.1).

Cardiopulmonary Risk Assessment

Assessment of cardiopulmonary reserve is especially difficult. Measurements traditionally employed to predict postthoracotomy pulmonary complications include ppFEV_1 , maximal oxygen consumption ($\text{VO}_2 \text{ max}$), and diffusing capacity for carbon monoxide (DL_{CO}) [18]. History, physical examination, and echocardiography will reflect cardiac functional status, but may not predict the response to the stress of pneumonectomy in the setting of major fluid shifts [19]. Patients with a history of recent myocardial infarction in the last 3 months or life-threatening arrhythmias would be considered for P/D rather than EPP.

Radiologic Studies

Computed tomography and magnetic resonance imaging (MRI) of the chest play an important role in assessing tumor invasion of the chest wall, vertebrae, diaphragm, and mediastinal structures. They are used for staging and/or to assess tumor resectability [20]. The anesthetic implications include safe placement of epidural catheters at the thoracic region, level of intravenous access, quantity of blood and blood products available, and the potential necessity for cardiopulmonary bypass during resection.

Anesthetic Considerations

Specific Anesthetic Issues for EPP

Beyond the standard management issues for pneumonectomy [21], important “EPP-specific” anesthesia concerns are shown in Table 28.3.

TABLE 28.3. Anesthetic issues for extrapleural pneumonectomy.

Significantly greater blood loss compared to pneumonectomy
More delicate management of intravascular fluid and blood components
Greater operative impairment of venous return
Greater danger of surgical disruption of major vascular structures
More complex and variable physiology of the nonoperative lung (restrictive and obstructive)
High probability for disruption of internal mammary artery coronary grafts (if present)
High probability of arrhythmias
Frequent “pseudo-ischemic” ST changes on ECG during wash phase
Greater potential for hemodynamic instability related to pericardial window and its patch
Greater postoperative pain and pulmonary dysfunction related to the larger incision

Lines and Monitors

Generous intravenous access is paramount and blood should be available in the operating room. If the superior vena cava is in jeopardy, lower extremity intravenous access is mandatory. A nasogastric tube aids posterior esophageal dissection intraoperatively and gastric decompression (and the prevention of gastric acid aspiration) postoperatively. Invasive monitors (arterial and central venous lines) are routine. The site of central venous access is important, as the potential for causing a pneumothorax in the nonoperative lung has to be weighed against injury to the subclavian vein during surgical dissection on the operative side.

Although PA catheters have potential interpretation pitfalls during pneumonectomy [22, 23], they may be useful for postoperative fluid and right heart management issues. Transesophageal echocardiography (TEE) is a more powerful and reliable monitor of right and left ventricular filling and function, and is a more sensitive monitor of myocardial ischemia, particularly during left EPP when the surgical incision precludes appropriate EKG lead placement. However, there is no direct evidence of improved outcome, and the cost and need of technical expertise make this tool worthwhile only in selected cases.

Choice of Anesthesia

No single anesthetic recipe is of proven superiority for either EPP or lung resection surgery in general. The priority for early extubation favors the use of short-acting modern inhalational and intravenous agents, with limited use of traditional parenteral narcotics.

Thoracic Epidural Analgesia

Compared to systemic opioids, thoracic epidural analgesia (TEA) reduces perioperative pulmonary [24] and cardiac complications [25, 26], including pulmonary infections, atelectasis, myocardial infarction, and the incidence of supraventricular tachyarrhythmias postthoracotomy. TEA is widely employed intra- and postoperatively for EPP. It also facilitates extubation

at the conclusion of surgery by providing dense analgesia without depression of sensorium or respiratory drive.

The sympatholytic effects of TEA may complicate hemodynamic management if dense blockade is imposed during or prior to the dissection phase of EPP. It is therefore common to initiate bolus dosing of the epidural catheter later in the surgery. Ultimately, solutions and infusion rates are individualized to address catheter insertion site, hypotension, pruritus, nausea, opioid tolerance, sedation, or other side effects.

One-Lung Anesthesia

Lung Isolation Techniques

Lung isolation to facilitate surgical exposure may be achieved using either a double-lumen endotracheal tube (DLT) or a bronchial blocker. For EPP, DLTs allow rapid ventilation or collapse of either lung, effective suctioning and uninterrupted lung isolation at the time of surgical crossclamp. We favor a left-sided DLT for a right EPP (and vice versa). There is no hardware present in the operative bronchus, and compared to a bronchial blocker, a left-sided DLT is less likely to be dislodged with surgical manipulation. Although right-sided DLTs have a smaller margin of safety (due to short right upper lobe anatomy), this is rarely an impediment to their effective use. When an anomalously high right upper lobe precludes an effective air seal at the bronchial cuff, this is easily remedied by passing a blocker down the tracheal lumen [27]. Blockers are principally used for left-sided EPP in patients with difficult airway anatomy, and withdrawn prior to stapling the bronchus in order to avoid accidental inclusion into the suture line.

Optimizing Oxygenation During OLV

Lung-protective (5–6 mL/kg tidal volume, limiting peak airway pressure <35 cmH₂O and plateau airway pressure <25 cmH₂O) ventilation and dependent lung positive end-expiratory pressure (PEEP) with the intention of limiting dependent lung volutrauma and atelectasis is important [28].

EPP patients, during OLV in the lateral decubitus position, often exhibit an element of restrictive physiology in the dependent lung imposed by the weight of the tumor and surgical pressure during dissection. Frequent large changes in compliance require vigilance to prevent high airway pressures or volumes (depending on the mode of ventilation). During intracavitary lavage, where a perfuse of cisplatin exerts weight on the mediastinum, PEEP is also important to prevent atelectasis. In addition, dependent lung pneumothorax may easily occur during dissection of large tumors and will require surgical decompression. The IOHC fluid may accumulate in the dependent thorax if the pleural defect is not adequately repaired.

Despite a greater propensity for dependent lung atelectasis and possibly increased nondependent lung shunt (inhibition of

hypoxic pulmonary vasoconstriction due to more vigorous surgical manipulation), hypoxemia during OLV for EPP is unusual. This is because the best predictor of oxygen desaturation during OLV is increased (>55% of cardiac output) blood flow to the operative lung, which is seldom the case in MPM [29].

Hemodynamic Management

Hypertension

Hypertension should be avoided during the dissection phase, as it will greatly exacerbate bleeding from the innumerable avulsed chest wall veins. It may also be an issue when the specimen is removed, and venous return to the heart is suddenly unimpeded.

Hypotension

This is more frequent, and its treatment should reflect its etiology whenever possible (Table 28.4). Reduced venous return is the most common mechanism, caused by mechanical pressure on the mediastinum during dissection, or torsion of great vessels. Critical phases of surgery when venous return is most threatened include the induction, dissection, and terminal repositioning phases. Vasodilation from hyperthermia during IOHC may occur as core temperatures not uncommonly exceed 38°C.

Induction

Preemptive vasoconstricting agents and judicious selection of induction agents/doses are particularly indicated for patients with large tumor burdens, large effusions, or radiographic evidence of cardiac or major vessel impingement. Often, the thoracic epidural test-dose effect is still peaking at the time of induction, potentially further increasing compensatory vasoconstrictor requirements.

TABLE 28.4. Causes of hypotension during EPP.

Common	Compression of heart or great vessels by tumor or surgical pressure/retraction Blood loss/inadequate fluid resuscitation Thoracic epidural sympathetic blockade
Uncommon	Air-trapping (“auto-PEEP”) Tension pneumothorax Drugs (vasodilators/negative inotropes) Right heart dysfunction/failure Cardiac herniation Tight pericardial patch Shifted mediastinum following closure Myocardial ischemia Arrhythmias Emolic events Transfusion reactions Drug reactions Sepsis

Dissection Phase

Venous return is impeded by blood loss, insensible losses, and variable degrees of compression from the tumor, retractors, and blunt dissection pressure. The temptation to correct venous return by enthusiastic crystalloid volume expansion is to be resisted. Judicious use of vasopressors, together with blood products when appropriate, will temporize until the specimen is removed. Communication with the surgeon during this phase is paramount, and a coordinated effort is necessary to maintain forward progress with acceptable hemodynamics. A low threshold for administration of blood during this phase often proves strategic. When the specimen is removed, venous return, hemodynamics, and respiratory compliance should normalize. Persistent hypotension at this stage suggests hypovolemia.

Repositioning and Emergence

Herniation of the heart (particularly with right EPP), with torsion of great vessels and circulatory arrest may abruptly occur upon resumption of the supine position at the end of surgery. Immediate return to the lateral position is the appropriate reflex response. This usually improves hemodynamic parameters while preparation for re-operation made if necessary.

The diagnosis is less obvious when only moderate hypotension occurs at this juncture. Culprits include partial cardiac herniation (loose or partially ruptured pericardial patch), tamponade (tight pericardial patch or retained pericardial effusion), inferior vena cava impingement (tight right diaphragmatic patch), hypovolemia, and deviated mediastinum, among others.

Reduced venous return is the common mechanistic denominator. A sluggish response to fluid boluses and vasopressors suggest that mechanical impediments to venous return should be ruled out before leaving the operating room. Aggressive bolus dosing of the epidural in anticipation of emergence may contribute to diagnostic confusion. A portable chest radiograph is usually helpful in ruling out partial cardiac herniation, or guiding medialization of the mediastinum by withdrawal of air from the chest drain. TEE may assist in the diagnosis.

Fluid Management

Average estimated intraoperative blood loss during EPP in the best of surgical hands is approximately 0.5–1.5 L. Most of this occurs in a gradual, continuous fashion during the processes of blunt separation of the parietal pleura from the chest wall, although catastrophic bleeding can occur from major vessels during dissection of the hilum or at the apex. Monitoring of the extent of blood loss requires vigilance and communication with the surgeons.

Antifibrinolytics have not been shown to reduce packed red blood cell requirements in EPP surgery [30]. As with any

pneumonectomy, excessive crystalloid is to be avoided as it may exacerbate the pulmonary edema of postlung resection acute lung injury. Fluid management thus becomes a balancing act in the setting of significant hemodynamic swings with intermittently moderate-to-major episodes of blood loss. This balance shifts in favor of more liberal fluid administration in patients receiving IOHC, out of concern for nephrotoxicity.

Central venous pressure measurements, PA occlusion pressures, or observance of respiratory variation on arterial line tracings may be unreliable indicators of intravascular volume during manipulation of weighty tumors, with the chest open to atmosphere. Attention to the surgical field (including the fullness of the heart), urine output, blood gas and hematocrit results, and occasionally TEE are helpful guides.

Postpneumonectomy Pulmonary Edema (PPE)

An emphasis is made on discriminating between hypovolemia and impairment of venous return out of concerns that unnecessary volume resuscitation may contribute to postpneumonectomy pulmonary edema (PPE). Pulmonary edema of the remaining lung following pneumonectomy occurs in 2–4% of patients and carries mortality in excess of 50% [31]. Statistics specifically applied to EPP have not been published, but the greater fluid shifts associated with EPP raise concern. It is apparent that in the presence of the increased pulmonary capillary permeability in acute lung injury, unnecessary crystalloid or colloid administration will exacerbate the degree of edema and hypoxemia. This is the basis for the widely adhered to practice of conservative (restrictive) fluid management for pneumonectomy patients [21], and highlights the importance of close attention to the matching of fluid administration to blood loss in EPP patients.

Cardiovascular Considerations

Arrhythmias

The incidence of supraventricular arrhythmias (SVA) after EPP is higher (21–44%) [2, 4, 5, 32] than for standard pneumonectomy (13–20%) [5, 32, 33]. Thoracic epidural blockade with bupivacaine has been shown to reduce the incidence of perioperative SVA compared to equi-analgesic epidural narcotics [26] and diltiazem has been shown to be moderately effective and safe in reducing postoperative atrial fibrillation (AF) and supraventricular tachycardia after thoracic surgery [34, 35]. However, there is currently inadequate evidence to recommend routine prophylaxis against AF for all patients undergoing lung surgery [36].

It is uncommon for routine prophylaxis against SVA for EPP, but important to avoid withdrawal of beta-adrenergic blocking drugs, if they are in use. Intraoperative arrhythmias

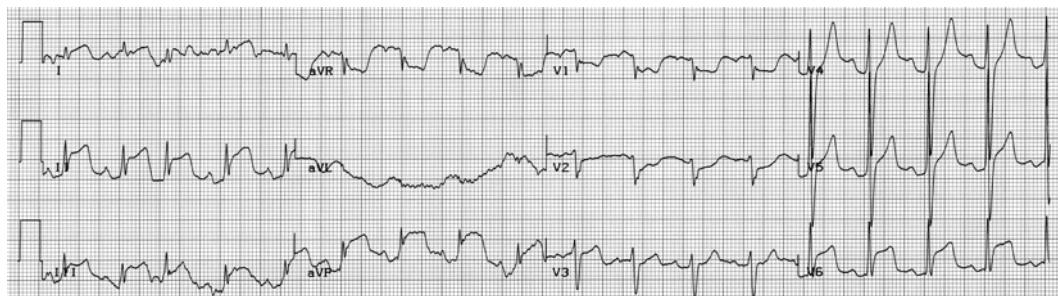


FIG. 28.4. The EKG obtained during wash phase with warm water, following removal of the specimen (including pericardium). Concurrent TEE revealed no global or regional wall motion abnormalities. The EKG rapidly normalized following termination of irrigation.

are generally triggered by mechanical irritation, and do not appear to predict postoperative SVA. EKG leads should be attached to a ready defibrillator to provide the capability of synchronized electrical cardioversion intraoperatively.

Myocardial Ischemia

Myocardial ischemia may be difficult to detect during EPP as alterations in the position of the heart relative to the surface EKG lead positions would be expected to alter their sensitivity. During left-sided thoracotomies, it is not practical to monitor lead V-5. When myocardial ischemia is suspected, TEE should be employed.

Dramatic ST segment elevations may occur during the wash phase. These tend to occur with irrigation, correct promptly with cessation, and are not associated with other hemodynamic alterations suggestive of myocardial ischemia (Fig. 28.4). These most likely represent nonischemic electrophysiologic changes related to focal myocardial warming or surface electrolyte changes [37]. No treatment is necessary unless they persist, produce hemodynamic instability, or are confirmed to be associated with wall motion abnormalities by TEE.

Perioperative Pain Management

There is increasing evidence that TEA with local anesthetics and opioids is superior in the control of dynamic pain, plays a key role in early extubation and mobilization, reduces postoperative pulmonary complications and has the potential to decrease the incidence of postthoracotomy pain syndrome. For EPP, although a bolus dose of local anesthetic may be administered prior to surgical incision, the risk of hemodynamic instability usually precludes continuous intraoperative dense neuraxial blockade. Nonetheless, it is vital to aggressively control acute postoperative pain [38, 39].

Preexisting pain related to mesothelioma is not uncommon and frequently treated with opioids. Tolerance may occur after 1–2 weeks of treatment and such patients present a challenge in terms of postoperative pain control and physiologic withdrawal. Patients on chronic opioids presenting for EPP would

generally receive an opioid-free epidural infusion, with additional patient-controlled systemic opioids prescribed to minimize the occurrence of withdrawal. Ketamine may be a useful adjunct [40].

Early Postoperative Considerations

Depending on center experience, majority of patients may be weaned and extubated in the operating room. This minimizes duration of positive pressure on the bronchial stump and avoids the potential problems of ventilator-associated alveolar barotrauma and infection. Prudence is advised in difficult or complicated EPP with increased transfusion requirement, or excessive fluid administration in the IOHC cases.

Management of the Ipsilateral Thoracic Space

In addition to the potential for cardiac herniation and its hemodynamic consequences (described earlier), rapid filling of the empty hemithorax with fluid, blood, or abdominal contents from a ruptured diaphragmatic patch can also compromise cardiorespiratory function. Air/fluid is removed from the chest drain at the end of surgery in an attempt to medialize the mediastinum. This is an imprecise process, and a chest radiograph is obtained on arrival in the ICU to assess mediastinal position. Intrathoracic pressure monitoring may guide intermittent fluid evacuation of the pneumonectomy space [41]. This prevents rapid accumulation resulting in respiratory compromise, whilst avoiding contralateral lung hyperexpansion, compromised venous return, and hypotension with excessive and/or rapid removal.

Other Issues Specific to EPP

- Patients who have undergone IOHC receive liberal fluids for the initial 24 h as part of the renal protection strategy (Table 28.1).
- Standard chest compression is ineffective in EPP patients because the mediastinum is dynamic and shifts to the empty hemithorax.

Conclusion

EPP is a radical and aggressive surgery, which presents a great challenge to the thoracic anesthesiologist. Besides standard anesthesia concepts for pneumonectomy, management involves an understanding of the technique of EPP, common intraoperative physiologic disruptions, and anticipated complications. Emerging multimodality treatments for MPM have additional anesthetic implications. One of those, IOHC, is discussed in the context of general EPP-specific anesthetic issues.

Clinical Case Discussion

A 50-year-old male is scheduled for right EPP. The diagnosis of mesothelioma was made on pleural biopsy and he has completed 6 cycles of chemotherapy. He is a nonsmoker and apart from well-controlled hypertension, he has no other significant co-morbidities.

Questions

1. Apart from routine preoperative assessment for pulmonary resection:
 - (a) Are any specialized cardiac and pulmonary function tests indicated?
 - Echocardiography commonly used to assess cardiac function.
 - Stress test only when history, examination, or echocardiography suggest significant cardiac disease.

- FEV₁, DL_{CO}, exercise capacity routinely assessed.
- Ventilation/perfusion scans recommended if FEV₁ < 2 L.
- Predicted postoperative FEV₁ < 1 L may preclude EPP.

- (b) What is the importance of radiologic investigations?
 - Surgical staging and tumor resectability.
 - Anesthetic implications include safe placement of epidural catheters at the thoracic region, level of intravenous access, quantity of blood and blood products available, and the potential necessity for cardiopulmonary bypass during resection.
2. How is an EPP different from pneumonectomy?
 - See Table 28.3.
3. What are the common causes of hypotension and the management strategies?
 - See Table 28.5.
4. How would the application of intraoperative intracavitary heated chemotherapy affect the anesthetic management?
 - Renal protective strategies should be employed (Table 28.1).
 - Restrictive physiology exhibited by EPP patients during one-lung ventilation is exacerbated by the weight of the perfusate, and PEEP is especially important to prevent atelectasis.
 - Fluid management is delicate balance between renal protection and the potential for exacerbation of acute lung injury in fluid overload.

TABLE 28.5. Hypotension during critical phases of surgery.

Phase	Mechanism(s)	Management strategy
Induction	Reduced venous return Vasodilation (induction agents, epidural) Exacerbation of tumor compressive effects by the decrease in FRC Loss of “thoracic pump” of spontaneous ventilation Positive pressure ventilation	Preemptive vasoconstricting agents and judicious selection of induction agents/ doses are particularly indicated for patients with large tumor burdens, large effusions, or radiographic evidence of cardiac or major vessel impingement
Dissection	Blood loss Insensible losses Variable degrees of compression from the tumor, retractors, and blunt dissection pressure	Communication with the surgeon is paramount Judicious use of vasopressors A low threshold for administration of blood and products when appropriate
Repositioning and emergence	Circulatory arrest Herniation of the heart (particularly with right EPP), with torsion of the SVC and IVC Moderate hypotension Partial cardiac herniation (loose or partially ruptured pericardial patch) Tamponade (tight pericardial patch) Hypovolemia Deviated mediastinum Aggressive bolus dosing of the epidural in anticipation of emergence	Immediate return to the lateral position A sluggish response to fluid boluses and vasopressors suggest that mechanical impediments to venous return should be ruled out A portable chest radiograph is usually helpful in ruling out partial cardiac herniation, or guiding medialization of the mediastinum

References

1. Butchart EG, Ashcroft T, Barnsley WC, Holden MP. Pleuro-pneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. *Thorax*. 1976;31:15–24.
2. Sugarbaker DJ, Jaklitsch MT, Bueno R, et al. Prevention, early detection, and management of complications after 328 consecutive extrapleural pneumonectomies. *J Thorac Cardiovasc Surg*. 2004;128:138–46.
3. Tilleman TR, Richards WG, Zellos L, et al. Extrapleural pneumonectomy followed by intracavitary intraoperative hyperthermic cisplatin with pharmacologic cytoprotection for treatment of malignant pleural mesothelioma: a phase II prospective study. *J Thorac Cardiovasc Surg*. 2009;138:405–11.
4. de Perrot M, McRae K, Anraku M, et al. Risk factors for major complications after extrapleural pneumonectomy for malignant pleural mesothelioma. *Ann Thorac Surg*. 2008;85:1206–10.
5. Harpole DH, Liptay MJ, DeCamp Jr MM, et al. Prospective analysis of pneumonectomy: risk factors for major morbidity and cardiac dysrhythmias. *Ann Thorac Surg*. 1996;61:977–82.
6. Opitz I, Kestenholz P, Lardinois D, et al. Incidence and management of complications after neoadjuvant chemotherapy followed by extrapleural pneumonectomy for malignant pleural mesothelioma. *Eur J Cardiothorac Surg*. 2006;29:579–84.
7. Sugarbaker DJ, Flores RM, Jaklitsch MT, et al. Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. *J Thorac Cardiovasc Surg*. 1999;117:54–63. discussion 63–55.
8. Krug LM, Pass HI, Rusch VW, et al. Multicenter phase II trial of neoadjuvant pemetrexed plus cisplatin followed by extrapleural pneumonectomy and radiation for malignant pleural mesothelioma. *J Clin Oncol*. 2009;27:3007–13.
9. de Perrot M, Feld R, Cho BC, et al. Trimodality therapy with induction chemotherapy followed by extrapleural pneumonectomy and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma. *J Clin Oncol*. 2009;27:1413–8.
10. Hartigan PM, Ng JM. Anesthetic strategies for patients undergoing extrapleural pneumonectomy. *Thorac Surg Clin*. 2004;14:575–83, xi.
11. Ng JM, Hartigan PM. Anesthetic management of patients undergoing extrapleural pneumonectomy for mesothelioma. *Curr Opin Anaesthesiol*. 2008;21:21–7.
12. Zellos L, Christiani DC. Epidemiology, biologic behavior, and natural history of mesothelioma. *Thorac Surg Clin*. 2004;14:469–77, viii.
13. Wagner JC, Sleggs CA, Marchand P. Diffuse pleural mesothelioma and asbestos exposure in the North Western Cape Province. *Br J Ind Med*. 1960;17:260–71.
14. Carbone M, Kratzke RA, Testa JR. The pathogenesis of mesothelioma. *Semin Oncol*. 2002;29:2–17.
15. Weder W, Opitz I, Stahel R. Multimodality strategies in malignant pleural mesothelioma. *Semin Thorac Cardiovasc Surg*. 2009;21:172–6.
16. Carroll N, Mohamed F, Sugarbaker P. Hyperthermic chemoperfusion, and postoperative chemotherapy: The National Cancer Institute and Washington Hospital Center experience. In: Pass H, Vogelzang N, Carbone M, editors. *Malignant mesothelioma: advances in pathogenesis, diagnosis and translational therapies*. New York: Springer; 2005. p. 732–54.
17. Lee JM, Sugarbaker DJ. Extrapleural pneumonectomy for diffuse malignant pleural mesothelioma and other diffuse pleural malignancies. In: Sugarbaker DJ, Bueno R, Krasna MJ, Mentzer SJ, Zellos L, editors. *Adult chest surgery*. New York: McGraw-Hill; 2009. p. 868–84.
18. Reilly Jr JJ. Evidence-based preoperative evaluation of candidates for thoracotomy. *Chest*. 1999;116:474S–6.
19. Amar D, Burt ME, Roistacher N, et al. Value of perioperative Doppler echocardiography in patients undergoing major lung resection. *Ann Thorac Surg*. 1996;61:516–20.
20. Gill RR, Gerbaudo VH, Sugarbaker DJ, Hatabu H. Current trends in radiologic management of malignant pleural mesothelioma. *Semin Thorac Cardiovasc Surg*. 2009;21:111–20.
21. Slinger P. Update on anesthetic management for pneumonectomy. *Curr Opin Anaesthesiol*. 2009;22:31–7.
22. Wittnich C, Trudel J, Zidulka A, Chiu RC. Misleading “pulmonary wedge pressure” after pneumonectomy: its importance in postoperative fluid therapy. *Ann Thorac Surg*. 1986;42:192–6.
23. Brister NW, Barnette RE, Kim V, Keresztury M. Anesthetic considerations in candidates for lung volume reduction surgery. *Proc Am Thorac Soc*. 2008;5:432–7.
24. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86:598–612.
25. Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. *Anesth Analg*. 2001;93:853–8.
26. Oka T, Ozawa Y, Ohkubo Y. Thoracic epidural bupivacaine attenuates supraventricular tachyarrhythmias after pulmonary resection. *Anesth Analg*. 2001;93:253–9.
27. Nino M, Body SC, Hartigan PM. The use of a bronchial blocker to rescue an ill-fitting double-lumen endotracheal tube. *Anesth Analg*. 2000;91:1370–1.
28. Slinger P. Pro: low tidal volume is indicated during one-lung ventilation. *Anesth Analg*. 2006;103:268–70.
29. Hurford WE, Kolker AC, Strauss HW. The use of ventilation/perfusion lung scans to predict oxygenation during one-lung anesthesia. *Anesthesiology*. 1987;67:841–4.
30. Bakaee F, Rice D, Correa AM, et al. Use of aprotinin in extrapleural pneumonectomy: effect on hemostasis and incidence of complications. *Ann Thorac Surg*. 2007;84:982–6.
31. Slinger PD. Perioperative fluid management for thoracic surgery: the puzzle of postpneumonectomy pulmonary edema. *J Cardiothorac Vasc Anesth*. 1995;9:442–51.
32. Passman RS, Gingold DS, Amar D, et al. Prediction rule for atrial fibrillation after major noncardiac thoracic surgery. *Ann Thorac Surg*. 2005;79:1698–703.
33. Roselli EE, Murthy SC, Rice TW, et al. Atrial fibrillation complicating lung cancer resection. *J Thorac Cardiovasc Surg*. 2005;130:438–44.
34. Amar D, Roistacher N, Burt ME, et al. Effects of diltiazem versus digoxin on dysrhythmias and cardiac function after pneumonectomy. *Ann Thorac Surg*. 1997;63:1374–81. discussion 1372–81.
35. Amar D, Roistacher N, Rusch VW, et al. Effects of diltiazem prophylaxis on the incidence and clinical outcome of atrial arrhythmias after thoracic surgery. *J Thorac Cardiovasc Surg*. 2000;120:790–8.

36. Dunning J, Treasure T, Versteegh M, Nashef SA. Guidelines on the prevention and management of de novo atrial fibrillation after cardiac and thoracic surgery. *Eur J Cardiothorac Surg.* 2006;30:852–72.
37. Brown MJ, Brown DR. Thoracic cavity irrigation: an unusual cause of acute ST segment increase. *Anesth Analg.* 2002;95: 552–4.
38. Obata H, Saito S, Fujita N, et al. Epidural block with mepivacaine before surgery reduces long-term post-thoracotomy pain. *Can J Anaesth.* 1999;46:1127–32.
39. Senturk M, Ozcan PE, Talu GK, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg.* 2002;94:11–5.
40. Suzuki M, Haraguti S, Sugimoto K, et al. Low-dose intravenous ketamine potentiates epidural analgesia after thoracotomy. *Anesthesiology.* 2006;105:111–9.
41. Wolf AS, Daniel J, Sugarbaker DJ. Surgical techniques for multimodality treatment of malignant pleural mesothelioma: extra-pleural pneumonectomy and pleurectomy/decortication. *Semin Thorac Cardiovasc Surg.* 2009;21:132–48.

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Key Points

- Pancoast tumors are very challenging lung cancers to treat because they involve vital structures including the brachial plexus, subclavian vessels, and spine.
- Multimodality management with induction chemoradiotherapy and surgery is now the standard of care for resectable Pancoast tumors.
- Preoperative planning between thoracic surgery, anesthesiology, and neurosurgery, including lung isolation technique, invasive hemodynamic monitoring, potential neurophysiologic monitoring, and a pain management plan is essential.
- Surgical approach is determined by the anatomic location of the tumor and is performed from either a posterior or anterior approach, or both.
- Because subclavian artery and vein involvement may require resection of these vessels, adequate intravascular monitoring and access must be planned.
- Pain control, pulmonary toilet, and physical therapy are key to achieving satisfactory postoperative recovery.

Introduction

Pancoast tumors, properly known as superior sulcus carcinomas, are a particularly challenging form of nonsmall cell lung cancer (NSCLC) to treat surgically because they commonly invade vital structures within and near the thoracic inlet. Invasion of the brachial plexus, subclavian vessels, and spine by direct tumor extension necessitates careful preoperative planning by surgeons and anesthesiologists. Originally

described in 1924 [1] and again in 1932 [2], by Henry K. Pancoast, a radiologist at the University of Pennsylvania, this subset of NSCLC was considered inoperable, and thus fatal, for nearly two decades until the late 1950s when the combination of radiotherapy and surgery offered some curative hope. Pancoast's description of an apical chest tumor associated with shoulder and arm pain, a Horner's syndrome, and atrophy of the hand muscles describes the constellation of signs and symptoms of the syndrome that has come to bear his name.

Anatomy of Pancoast Tumors

The Superior Sulcus

An understanding of the anatomy of the superior sulcus is essential for the diagnosis and treatment of Pancoast tumors. The pulmonary sulcus is anatomically synonymous with the costovertebral gutter (the junction of the ribs to the vertebral column) in the posterior aspect of the chest, and spans the thorax from the first rib down to the diaphragm. The superior pulmonary sulcus encompasses the most apical aspect of the gutter. Thus, a Pancoast tumor is a NSCLC arising in the apex of the lung located within the costovertebral gutter that causes constant pain due to local invasion into any of the following structures: the chest wall, spine, intercostal nerves, brachial plexus, subclavian vessels, sympathetic trunk, and stellate ganglion. The classic symptoms associated with Pancoast tumors are directly related to the structures compromised by this apicocostovertebral tumor. For instance, shoulder pain is due to a combination of local invasion into the chest wall and

intercostal nerves. The arm pain produced by the tumor signifies invasion into the C8-T1 nerve roots. Unrelenting pain down the ulnar surface of the forearm and fourth and fifth fingers results from C8 involvement and pain in the ulnar aspect of the arm to the elbow represents T1 invasion. A Horner's syndrome is produced by tumor impingement on the sympathetic chain and stellate ganglion, structures located in the posterior aspect of the superior sulcus. Because some superior sulcus NSCLC involve the subclavian vessels rather than the paravertebral area, the classification of a NSCLC as a Pancoast tumor has expanded to include all tumors of the superior sulcus whether or not there is involvement of the brachial plexus or stellate ganglion. NSCLCs located in the apex of the chest that involve the second rib or lower are not considered Pancoast tumors and are generally termed apical lung cancers.

The Thoracic Inlet

The thoracic inlet is perhaps the most important anatomic area to understand when treating Pancoast tumors because this anatomic region encompasses crucial neurovascular structures and musculoskeletal elements and symptoms are directly related to the location of these tumors and their involvement of these structures. The surgical resection of superior sulcus tumors requires an intricate knowledge of these anatomic relationships and the consequences of resection, need for reconstruction, and risks of injury to the patient. The thoracic inlet is the superior aperture of the thoracic cavity bounded by the first thoracic vertebra (T1) posteriorly, the first ribs laterally, and the superior border of the manubrium anteriorly (Fig. 29.1) [3]. The root of the neck lies just superior to the thoracic inlet with the brachial plexus located in a superolateral position between the anterior and middle scalene muscles, superior to the first rib.

The thoracic inlet can be separated into three distinct compartments based on the insertion of the anterior and middle scalene muscles on the first rib and the posterior scalene muscle on the second rib. The anterior compartment is

located in front of the anterior scalene muscle and contains the sternocleidomastoid and omohyoid muscles, the subclavian and internal jugular veins and their branches. Tumors in this location tend to invade the first intercostal nerve and first rib resulting in pain in the upper and anterior chest wall (Fig. 29.2a, b). The middle compartment, located between

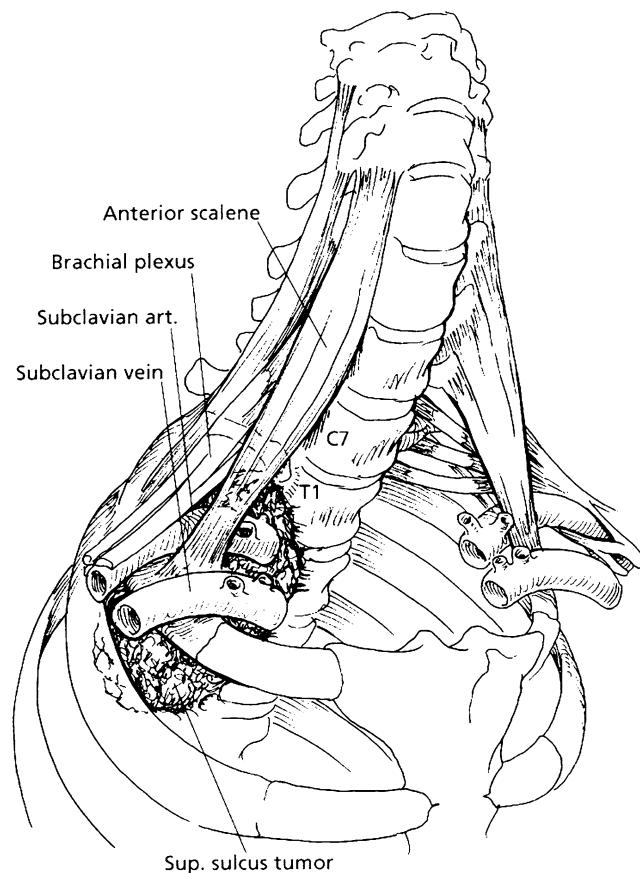


FIG. 29.1. The structure of the thoracic inlet (reprinted from Nesbitt et al. [3], with permission).

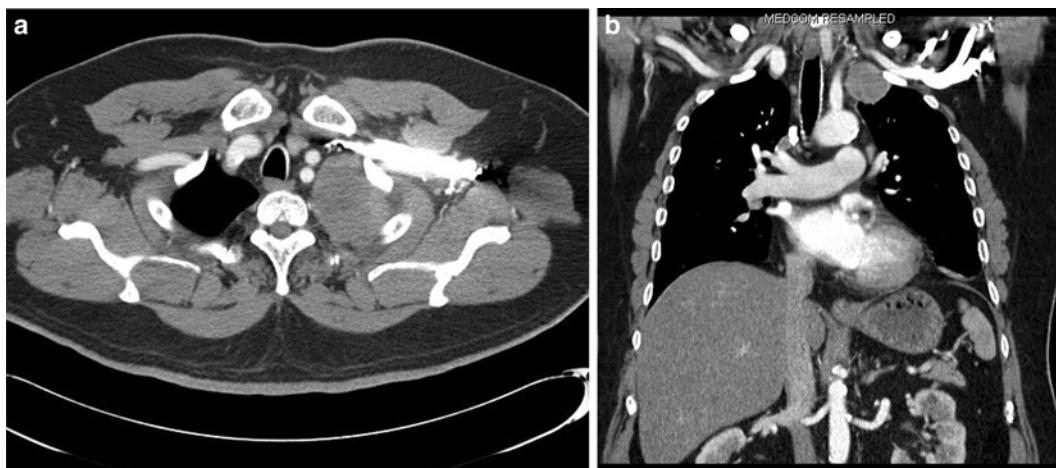


FIG. 29.2. (a, b) Left Pancoast tumor, clinical stage T3 filling superior sulcus but not invading spine or involving subclavian vessels (a). The extent of the tumor is also well defined on the coronal view of the CT scan.

the anterior and middle scalene muscles, includes the subclavian artery, the trunks of the brachial plexus, and the phrenic nerve that lies on the anterior surface of the anterior scalene muscle (Fig. 29.3). Tumors found in the middle compartment may invade the anterior scalene muscle, the phrenic nerve, the subclavian artery, and the trunks of the brachial plexus and middle scalene muscle. These tumors tend to present with signs and symptoms related to direct compression or infiltration of the brachial plexus such as pain and paresthesias in the ulnar distribution. The posterior compartment contains the nerve roots of the brachial plexus, the stellate ganglion and the vertebral column, the posterior aspect of the subclavian artery, the paravertebral sympathetic chain, and the prevertebral musculature. Tumors in the posterior inlet can invade the transverse processes and vertebral bodies, as well as the spinal foramina (Fig. 29.4a, b) and be associated with neuromuscular

pathology such as a Horner's syndrome (ptosis, miosis, and anhydrosis), and brachial plexopathy (weakness of the intrinsic muscles of the hand), paralysis of the flexors of the digits resembling a "claw hand," and diminished sensation over the medial side of the arm, forearm, and hand (related to C8 and T1 destruction).

Initial Assessment

Superior sulcus tumors or masses associated with chest and arm pain may be due to other pathologic processes including infectious conditions like tuberculosis, or other malignant disorders including lymphoma, primary chest wall tumors, or metastatic disease from other neoplasms (Table 29.1) [4]. Therefore a diagnosis of NSCLC must be confirmed before instituting definitive therapy. This is best accomplished by transthoracic fine-needle aspiration (FNA).

Once a diagnosis of NSCLC has been made, the extent of disease should be evaluated before surgical resection is considered. Patients are evaluated with a computed tomography (CT) of the chest and upper abdomen with intravenous contrast, including the adrenals, whole-body positron emission tomography (FDG-PET), and a brain magnetic resonance imaging (MRI) to exclude metastatic disease in extrathoracic sites as well as in the mediastinum. Pancoast tumors are, by definition, at least stage IIB lung cancers, with a significant risk of mediastinal nodal involvement in 10–20% of patients [5]. Because Pancoast tumors with mediastinal nodal involvement (N2 or N3 disease) have markedly worse survival than those that are N0 or N1, further staging by endobronchial ultrasound (EBUS) and/or mediastinoscopy should be considered if CT or positron emission tomography (PET) suggest mediastinal nodal disease [6].

Due to the unique anatomic position of these tumors, diagnostic imaging with contrast MRI plays an essential role in defining the extent of local invasion and thus, resectability [7, 8]. The brachial plexus, subclavian vessels, vertebrae, and

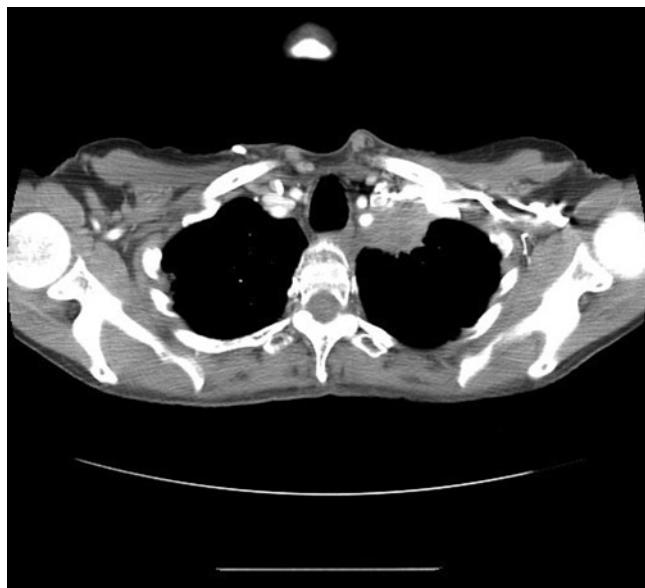


FIG. 29.3. Anteriorly located left Pancoast tumor involving subclavian vessels requiring anterior "Darteville" approach to resection.

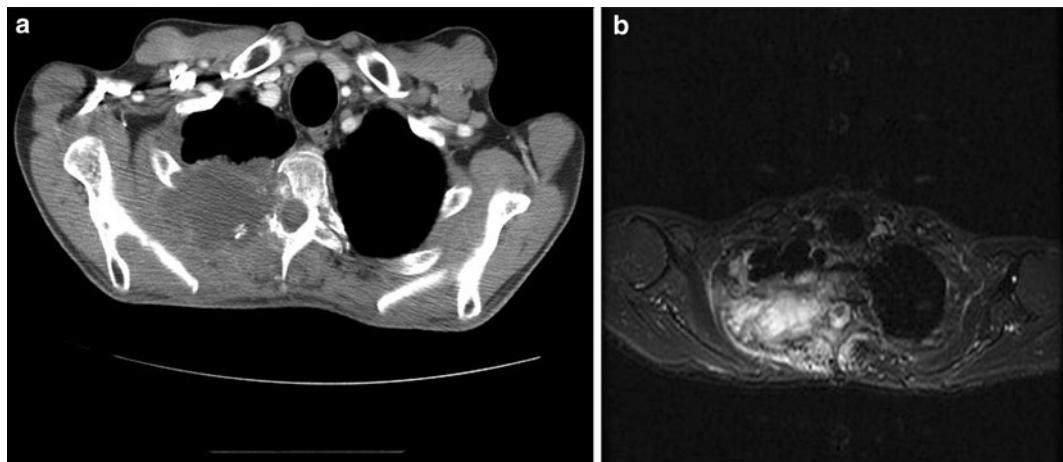


FIG. 29.4. (a, b) Right Pancoast tumor invading chest wall and destroying adjacent vertebral body as shown on CT (a) and MR (b) scans.

TABLE 29.1. Causes of Pancoast's syndrome.

Neoplastic	
Lung neoplasms	Primary bronchogenic Adenoid cystic carcinomas Hemangiopericytoma Mesothelioma
Metastatic neoplasms	Laryngeal cancer Cervical cancer Uroepithelial cancer Thyroid cancer
Hematologic neoplasms	Lymphoma Plasmacytoma
Infectious	
Bacterial	Staphylococcal pneumonia Pseudomonal pneumonia Actinomycosis
Fungal	Aspergillosis Cryptococcosis Tuberculosis
Parasitic	Hydatid cyst

neural foramina are best visualized with this modality. T1 involvement and resection is well tolerated, but resection of the C8 nerve root and lower trunk of the brachial plexus generally leads to permanent loss of intrinsic hand function and lower arm function. Radiographic evidence of spine involvement, or neurologic symptoms and signs suggestive of nerve root or brachial plexus pathology, necessitate joint evaluation of these patients by a thoracic surgeon and a spine surgeon. At Memorial Sloan-Kettering Cancer Center, the treatment of all Pancoast tumors is planned jointly by the thoracic surgeon and spine neurosurgeon.

Multimodality Treatment

From the late 1950s to the present day, the therapeutic approach to Pancoast tumors has evolved into a multidisciplinary and multimodality treatment regimen that includes induction chemoradiotherapy and resection. In 1956, Chardack and MacCallum described successful treatment of a Pancoast tumor by en-bloc resection of the right upper lobe, chest wall, and nerve roots followed by adjuvant radiotherapy leading to a 5-year survival in that patient [9]. In 1961, Shaw et al. reported their experience with a patient who presented with Pancoast's syndrome but became symptom-free after 30 Gy of radiotherapy and then went on to a successful resection. This treatment strategy was then applied to 18 more patients with good local control and better than expected long-term survival [10]. The Shaw and Paulson approach, based on induction radiotherapy and en-bloc resection, then became the standard of care for Pancoast tumors. During the next 30 years, the basic approach to treatment remained unchanged. The largest retrospective study published to date, from Memorial Sloan-Kettering Cancer Center, defined negative prognostic factors including mediastinal lymph node metastases, N2 disease,

vertebral and subclavian vessel involvement, and incomplete resection [6]. Complete (R0) resection was achieved in only 64% of patients with T3N0 disease and 39% of patients with T4N0 disease, and locoregional relapse was the most common site of tumor recurrence. Anatomic lobectomy was associated with a better outcome than sublobar resection and intraoperative brachytherapy did not enhance overall survival [11]. This retrospective study documented the results of "standard" treatment for resectable Pancoast tumors during a nearly 40-year period and emphasized the need for novel approaches that would improve both local control and survival.

Because combined modality therapy was increasingly being used for other locally advanced NSCLC subsets (e.g., stage IIIA (N2) disease) [12], induction chemoradiotherapy followed by surgical resection was studied in a large North American prospective multi-institutional phase II trial for Pancoast tumors (T3-4 N0-1M0 tumors) [13]. A total of 110 eligible patients were enrolled on this study and received induction therapy using 2 cycles of cisplatin and etoposide chemotherapy along with 45 Gy of concurrent radiotherapy. Patients with stable or responding disease then underwent thoracotomy and resection followed by 2 more cycles of chemotherapy. Induction therapy was well tolerated allowing 75% of enrolled patients to go on to thoracotomy. R0 resection was achieved in 91% of T3 and 87% of T4 tumors. Approximately one-third of patients had no residual viable tumors, one-third had minimal residual microscopic disease, and one-third had gross residual tumor on final pathology. Patients who had a R0 resection experienced a 53% survival at 5 years and the most common sites of relapse were distant rather than locoregional. Several more recent studies, including a multicenter prospective clinical trial from Japan, confirmed these results [14-17] and established induction chemoradiotherapy and surgery as standard care for resectable Pancoast tumors.

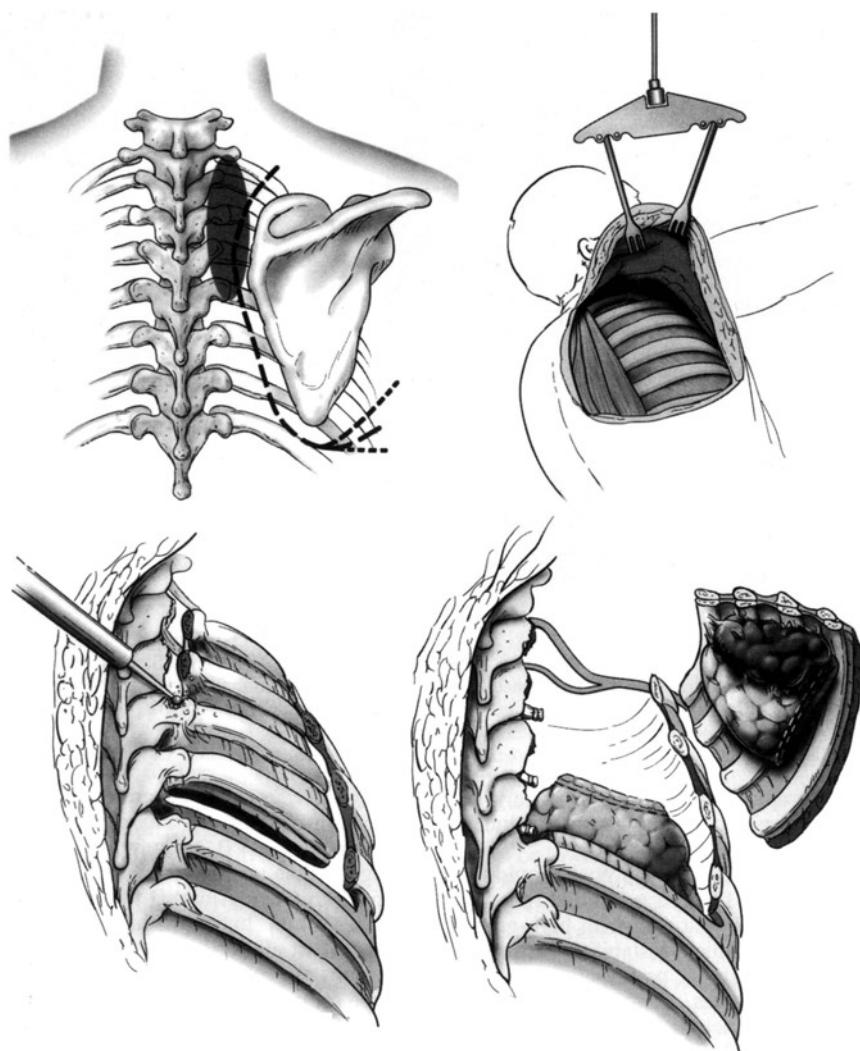
Surgical Approaches to Resection

The goal of any cancer operation is the complete resection of the tumor with negative margins. In the case of Pancoast tumors, due to their unique location at the apex of the chest and at times their involvement of the thoracic inlet, complete resection is challenging and usually includes the upper lobe, involved chest wall with or without the subclavian vessels, portions of the vertebral column and T1 nerve root, and dorsal sympathetic chain. Pancoast tumors may be approached through an extended high posterolateral thoracotomy incision (Paulson's approach) or through an anterior approach popularized by Darteville.

Posterior Approach

The patient is positioned in the lateral decubitus position but rotated slightly anteriorly, to provide exposure to the paravertebral region [18]. A standard posterolateral thoracotomy

FIG. 29.5. Artist's illustration of a posterolateral thoracotomy. *Upper left*: incision is made midway between the spinous processes and medial border of the scapula and extending over the inferior border. *Upper right*: The rhomboid and levator scapulae muscles are sectioned to elevate the scapula from the chest wall by using a mammary self-retaining retractor. *Lower left*: The paraspinal muscles are dissected to expose the junction of the laminae and transverse processes. The drill is used to resect the transverse processes distal to the pedicle to expose the neural foramen. For a Type C resection, the laminae, facet joints, and pedicles are resected to expose the lateral dura. *Lower right*: the chest wall is then pushed forward, and the nerve roots are ligated at the distal neural foramen. En-bloc chest wall and tumor resection are accomplished (reprinted from Bilsky et al. [18], with permission).



is performed in the fifth intercostal and the chest explored to make sure that there is no evidence of metastatic disease. If the tumor appears resectable, the incision is extended superiorly to the base of the neck following a line midway between the spinous process and the edge of the scapula (Fig. 29.5). Extension of the incision anteriorly around the anterior border of the scapula up toward the axilla can also be used to enhance exposure. The scapula is elevated away from the chest wall with either a rib-spreading retractor or internal mammary retractor with good visualization of the apex of the chest. The scalene muscles are detached from the first and second ribs and the first rib exposed. Involved ribs are divided anteriorly to allow for a 4-cm margin away from the tumor. Care is taken to visualize and control the intercostal neurovascular bundle. To facilitate the posterior dissection, the erector spinae muscles are retracted off the thoracic spine allowing for visualization of the costovertebral gutter. To provide an adequate posterior margin, the transverse processes and rib heads are usually resected en-bloc. Intercostal

nerves are meticulously ligated before division to prevent leak of cerebrospinal fluid. Bleeding near the neural foramina is carefully controlled with bipolar electrocautery. The T1 nerve root is examined for tumor involvement and ligated if needed. Division of the T1 nerve root may cause mild paresis of the intrinsic muscles of the hand but division of the C8 nerve root will result in permanent paralysis. Frozen sections are used liberally during the operation to determine the necessary extent of resection. After the chest wall resection is completed, the detached chest wall is allowed to fall into the chest cavity and an upper lobectomy and mediastinal lymph node dissection is completed in the standard fashion. Reconstruction of the chest wall is not necessary unless the defect created is larger than the first three ribs in which case the angle of the scapula can herniate into the chest cavity causing pain and impaired movement. If a chest wall reconstruction is needed, a 2-mm thick Gore Tex patch (WL Gore, Flagstaff, AZ, USA) is sutured to the margins of resection under tension and secured in place.

Vertebral Body and Epidural Tumors

Vertebral body invasion by Pancoast tumors is not necessarily a contraindication to surgical resection. The development of better instrumentation for spine stabilization now permits a more aggressive approach to these tumors [18, 19]. Currently, with multimodality therapy, T4 lesions with vertebral body or epidural extension can be considered for resection with curative intent. At Memorial Sloan-Kettering Cancer Center, spine MRI images are used to divide tumors into four classes, A–D, based on the degree of spinal column and neural tube involvement [18]. Class A and B tumors are T3 lesions that are amenable to complete R0 resection. Class A tumors involve only the periosteum of the vertebral bodies and class B tumors are limited to the rib heads and distal neural foramina. Class C and D tumors are T4 lesions that are not amenable to en-bloc resection but can still be completely resected. Class C tumors extend into the neural foramina, have limited or no vertebral body involvement but do have unilateral epidural compression. Class D tumors involve the vertebral column, either the vertebral body and/or lamina with or without epidural compression. Class A, B and some class C tumors can be approached through a posterolateral thoracotomy. A high-speed drill is used to remove involved vertebral bodies. The posterior longitudinal ligament is removed and provides a margin on the anterior dura. The disk spaces adjacent to the tumor are exenterated in order to aid in spinal fixation. Anterior reconstruction alone is sufficient for resections of one to two vertebral bodies. Autologous bone from the iliac crest or nondiseased rib, allograft fibula, or methymethacrylate with Steinman pins can all be used for reconstruction.

Class D tumors that involve the posterior elements (spinous process, laminae, and pedicles) are resected through a combined anterior/posterior approach. Patients are positioned prone and a posterior midline incision made. The involved areas of the spinous process, laminae, and pedicles are resected. Epidural tumor is dissected off the dura and a multilevel resection of affected nerve roots done. Posterior fixation is accomplished in order to maintain coronal and sagittal stability (Fig. 29.6). If soft tissue over the reconstruction is inadequate, muscle flap rotation by a plastic surgeon can be done to reduce the risk of skin breakdown and infection of the spine hardware [19, 20]. Once the posterior resection and reconstruction is complete, the incision is closed, the patient turned to the lateral decubitus position, a posterolateral thoracotomy performed and the lung and chest wall resection completed.

Anterior Approaches

Pancoast tumors that involve the subclavian vessels are best approached anteriorly. Although several different approaches have been described [21–26] the anterior transcervical approach, originally described by Darteville and modified by others [27], is considered the standard approach for this subset of Pancoast tumors.

The patient is positioned supine with the neck hyperextended and the head turned to the opposite side of the lesion [28, 29].

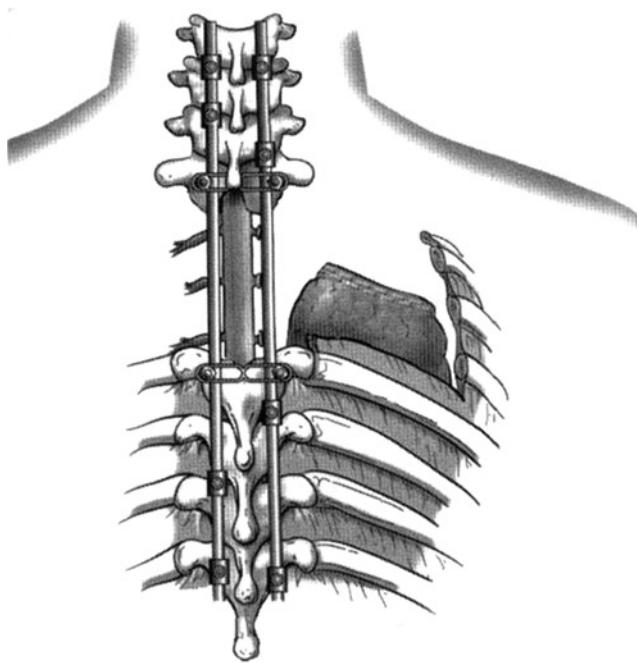


FIG. 29.6. Artist's illustration depicting a posterolateral transpedicular approach for Class D tumor with bilateral posterior segmental fixation (reprinted from Bilsky et al. [18], with permission).

An inverted L-shaped incision is carried down the anterior border of the sternocleidomastoid muscle and extended below the clavicle to the level of the second intercostal space, then turned horizontally following a parallel line below the clavicle to the deltopectoral groove (Fig. 29.7). The sternal attachment of the sternocleidomastoid is divided along with the insertion of the pectoralis major. A myocutaneous flap is then folded laterally exposing the thoracic inlet. The scalene fat pad is excised and sent for frozen section to determine lymph node involvement. If the tumor is deemed resectable, the upper part of the manubrium is divided and the incision carried into the second intercostal space via an L-shaped incision. The involved section of the subclavian vein is resected but not reconstructed (collateral venous flow around this area being sufficient).

Next, the anterior scalene muscle is divided either at its insertion onto the first rib. The phrenic nerve is identified and preserved. The subclavian artery is resected and reconstructed with a 8- or 10-mm polytetrafluoroethylene (PTFE) graft (Fig. 29.8). The middle scalene muscle is detached above its insertion on the first rib to expose the C8 and T1 nerve roots. These are dissected in a lateral to medial direction up to the confluence of the lower trunk and brachial plexus. The ipsilateral prevertebral muscles and paravertebral sympathetic chain and stellate ganglion are then resected off the anterior aspect of the vertebral bodies of C7 and T1. The T1 nerve root is commonly divided just lateral to the T1 intervertebral foramen.

Attention can now be placed on the chest wall resection. The anterolateral arch of the first rib is divided at the costochondral junction and the second rib is divided at its midpoint. The third rib is dissected on its superior border in a posterior direction

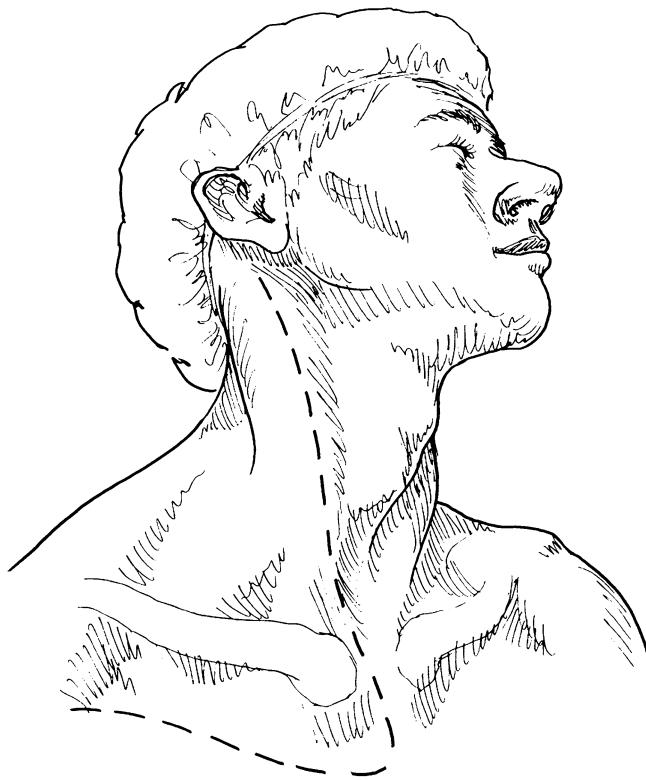


FIG. 29.7. An anterior trans cervical incision is made and curved under the head of the clavicle in an L-fashion (reprinted from Nesbitt et al. [3], with permission).

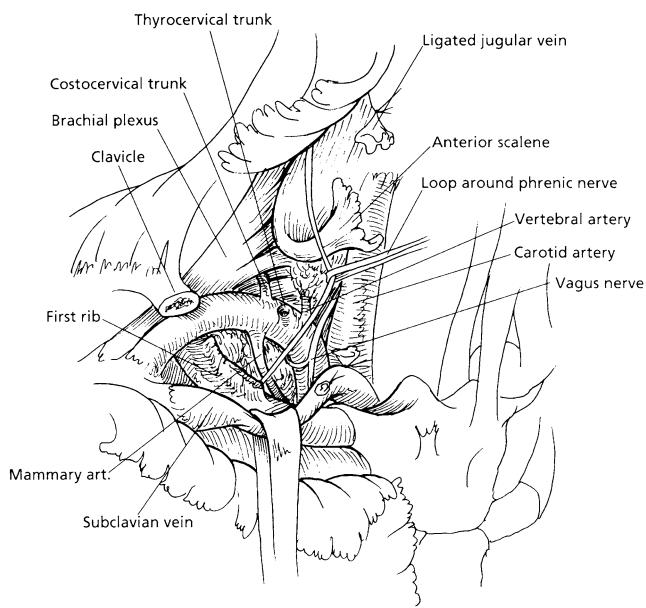


FIG. 29.8. The phrenic nerve and subclavian vein are retracted. The anterior scalene muscle is divided to expose the subclavian artery (reprinted from Nesbitt et al. [3], with permission).

toward the costovertebral angle and the first two through three ribs are disarticulated from the transverse processes. From this cavity, an upper lobectomy is completed. If exposure for the

lobectomy and chest wall resection is inadequate, the anterior incision is closed and the patient turned into the lateral decubitus position. The remainder of the resection can then be performed via a posterolateral thoracotomy incision.

Anesthetic Considerations

Lung isolation technique with a double-lumen tube or bronchial blocker can be used depending on surgeon's and anesthesiologist's experience and preference. Intra-arterial blood pressure monitoring and large bore IV access should be placed on the side opposite to the tumor. If there is potential for SVC or innominate vein resection, venous access via the femoral region or lower extremity is advisable. Central venous catheterization on the nonoperative side maybe considered if adequate IV access is unavailable or if the patient's cardiovascular reserve is limited and perioperative use of vasoactive agents is anticipated. There are sparse data on whether to employ neurophysiologic monitoring during resection of Pancoast tumors. In the case of thoracic and thoracoabdominal aortic aneurysm repair where spinal cord ischemia is a devastating complication, a recent prospective series of 233 patients demonstrated that normal somatosensory and motor-evoked potential monitoring intraoperatively had a strong negative predictive value indicating that patients without signal loss are unlikely to awake with a neurologic deficit, whereas irreversible changes on monitoring were significantly associated with immediate postoperative neurologic deficit [30]. If spine stabilization is required, it is our practice to employ somatosensory and motor-evoked potential monitoring intraoperatively. The cause of reversible changes during surgery is often due to compression of segmental spinal arteries or spinal cord hypoperfusion. Both of these situations can lead to spinal cord infarction unless corrected usually by pharmacologically elevating the patient's blood pressure. During neurophysiologic monitoring, it is customary to employ minimal inhalation anesthesia balanced by total intravenous anesthetic regimens with Bispectral brain monitoring when feasible. Since lobectomy or pneumonectomy is needed in some cases, judicious fluid administration is recommended due to the risk of postoperative pulmonary edema and respiratory distress in these patients. Pain control must be accomplished, usually with an epidural catheter, in order to aid in early mobilization, pulmonary toilet, and chest physiotherapy. Patients with preoperative pain may be taking significant amount of opioid analgesics prior to surgery and will likely have opioid tolerance, thus requiring a careful multimodal approach by a pain specialist that might include drugs against neuropathic pain, intravenous ketamine, nonsteroidal anti-inflammatory agents, and continuous nerve block in extreme cases.

Postoperative Considerations

The most common postoperative complications are respiratory (atelectasis, pneumonia) and are related to the extent of the incision and associated pain. Adequate pain control

and intensive respiratory care are pivotal to preventing these problems. The patient should be mobilized the first post-operative day with attention to chest physiotherapy. Awake bronchoscopic suctioning may be required to clear retained secretions in those patients who have an ineffective cough. Other postoperative complications are those usually seen after pulmonary resection, including supraventricular cardiac arrhythmias, bleeding, wound infection, or empyema. Chylothoraces can occur in patients who had had extensive resections in the paravertebral region (either right- or left-sided). Infection of the hardware used for spine stabilization is an uncommon but very serious adverse event that may require reoperation and drainage. Leak of cerebrospinal fluid is also rare but can be an extremely serious complication requiring reoperation. It is related to inadequate closure of the dura most frequently along the intercostal nerve roots at the level of the spinal foramina.

Clinical Case Discussion (Fig. 29.4a)

Case: A 50-year-old man with a recent history of dyspnea on exertion and recurrent pneumonias for the past year is scheduled for surgical resection of a large apical right lung mass. He is a former 40 pack-year smoker. He has moderately severe but clinically stable multiple sclerosis. He reports pain in his shoulder radiating down his arm, but has normal strength and function in his right hand. CT scan, PET Scan, and MRI have been done and suggest no evidence of metastatic disease but extension into the paravertebral area and spine.

Questions

1. What position(s) will the patient be in for resection?
2. What is your plan for intravascular monitoring and access?
3. Do you think a chest wall reconstruction will be necessary?
4. If the vertebral bodies are involved, what other exposure is necessary?
5. What strategy do you have for fluid management and post-operative pain control?

Discussion

Based on the history and preoperative imaging, this patient has a superior sulcus tumor, or Pancoast tumor, involving vital structures in the thoracic inlet and spine. A combined posterior and anterior approach will be necessary for complete resection (see description in text). The patient will be placed prone for the spine resection and stabilization. Once that is completed, the patient will be rotated into the lateral decubitus position and a posterolateral thoracotomy performed to complete the lobectomy and chest wall resection and reconstruction.

References

1. Pancoast HK. Importance of careful roentgen-ray investigations of apical chest tumors. *J Am Med Assoc.* 1924;83:1407–11.
2. Pancoast HK. Superior pulmonary sulcus tumor. *J Am Med Assoc.* 1932;99:1391–6.
3. Nesbitt JC, Wind GG, Rusch VW, Walsh GL. Superior sulcus tumor resection. In: Nesbitt JC, Wind GG, Deslauriers J, Faber LP, Ginsberg RJ, Moores DWO, et al., editors. *Thoracic surgical oncology.* Philadelphia: Lippincott Williams & Wilkins; 2003. p. 162–93.
4. Arcasoy SM, Jett JR. Superior pulmonary sulcus tumors and Pancoast's syndrome. *N Engl J Med.* 1997;337:1370–6.
5. Dettberbeck FC. Changes in the treatment of Pancoast tumors. *Ann Thorac Surg.* 2003;75:1990–7.
6. Rusch VW, Parekh KR, Leon L, et al. Factors determining outcome after surgical resection of T3 and T4 lung cancers of the superior sulcus. *J Thorac Cardiovasc Surg.* 2000;119:1147–53.
7. McLoud TC, Filion RB, Edelman RR, Shepard JA. MR imaging of superior sulcus carcinoma. *J Comput Assist Tomogr.* 1989;13:233–9.
8. Freundlich IM, Chasen MH, Varma DG. Magnetic resonance imaging of pulmonary apical tumors. *J Thorac Imaging.* 1996;11:210–22.
9. Chardack WM, MacCallum JD. Pancoast tumor (five year survival without recurrence or metastases following radical resection and postoperative irradiation). *J Thorac Surg.* 1956;31:535–42.
10. Shaw RR, Paulson DL, Kee Jr JL. Treatment of the superior sulcus tumor by irradiation followed by resection. *Ann Surg.* 1961;154:29–40.
11. Ginsberg RJ, Martini N, Zaman M, et al. Influence of surgical resection and brachytherapy in the management of superior sulcus tumor. *Ann Thorac Surg.* 1994;57:1440–5.
12. Albain KS, Rusch VW, Crowley JJ, et al. Concurrent cisplatin/etoposide plus chest radiotherapy followed by surgery for stages IIIA (N2) and IIIB non-small cell lung cancer: mature results of Southwest Oncology Group Phase II study 8805. *J Clin Oncol.* 1995;13:1880–92.
13. Rusch VW, Giroux DJ, Kraut MJ, et al. Induction chemoradiation and surgical resection for superior sulcus non-small cell lung carcinomas: long-term results of Southwest Oncology Group trial 9416 (Intergroup trial 0160). *J Clin Oncol.* 2007;25:313–8.
14. Marra A, Eberhardt W, Pöttgen C, et al. Induction chemotherapy, concurrent chemoradiation and surgery for Pancoast tumour. *Eur Respir J.* 2007;29:117–27.
15. Fischer S, Darling G, Pierre AF, et al. Induction chemoradiation therapy followed by surgical resection for non-small cell lung cancer (NSCLC) invading the thoracic inlet. *Eur J Cardiothorac Surg.* 2008;33:1129–34.
16. Kunitoh H, Kato H, Tsuboi M, et al. Phase II trial of preoperative chemoradiotherapy followed by surgical resection in patients with superior sulcus non-small cell lung cancers: report of Japan Clinical Oncology Group Trial 9806. *J Clin Oncol.* 2008;26:644–9.
17. Kappers I, van Sandick JW, Burgers JA, et al. Results of combined modality treatment in patients with non-small cell lung cancer of the superior sulcus and the rationale for surgical resection. *Eur J Cardiothorac Surg.* 2009;36:741–6.
18. Bilsky MH, Vitaz TW, Boland PJ, Bains MS, Rajaraman V, Rusch VW. Surgical treatment of superior sulcus tumors with

- spinal and brachial plexus involvement. *J Neurosurg.* 2002; 97(3 Suppl):301–9.
19. Gandhi S, Walsh GL, Komaki R, et al. A multidisciplinary surgical approach to superior sulcus tumors with vertebral invasion. *Ann Thorac Surg.* 1999;68:1778–85.
20. Bolton WD, Rice DC, Goodyear A, et al. Superior sulcus tumors with vertebral body involvement: a multimodality approach. *J Thorac Cardiovasc Surg.* 2009;137(6):1379–87.
21. Masaoka A, Ito Y, Yasumitsu T. Anterior approach for tumor of the superior sulcus. *J Thorac Cardiovasc Surg.* 1979;78:413–5.
22. Niwa H, Masaoka A, Yamakawa Y, Fukai I, Kiriyma M. Surgical therapy for apical invasive lung cancer: different approaches according to tumor location. *Lung Cancer.* 1993;10:63–71.
23. Nazari S. Transcervical approach (Darteville technique) for resection of lung tumors invading the thoracic inlet, sparing the clavicle. *J Thorac Cardiovasc Surg.* 1996;112:558–60.
24. Marshall MB, Kucharczuk JC, Shrager JB, Kaiser LR. Anterior surgical approaches to the thoracic outlet. *J Thorac Cardiovasc Surg.* 2006;131(6):1255–60.
25. Grunenwald D, Spaggiari L, Girard P, Baldeyrou P. Transmanubrial approach to the thoracic inlet. *J Thorac Cardiovasc Surg.* 1997;113:958–9.
26. Klima U, Lichtenberg A, Haverich A. Transmanubrial approach repropposed: reply. *Ann Thorac Surg.* 1999;68:1888.
27. Darteville PG, Chapelier AR, Macchiarini P, et al. Anterior transcervical-thoracic approach for radical resection of lung tumors invading the thoracic inlet. *J Thorac Cardiovasc Surg.* 1993;105:1025–34.
28. Macchiarini P. Resection of superior sulcus carcinomas (anterior approach). *Thorac Surg Clin.* 2004;14:229–40.
29. Fadel E, Missenard G, Chapelier A, et al. En bloc resection of non-small cell lung cancer invading the thoracic inlet and intervertebral foramina. *J Thorac Cardiovasc Surg.* 2002;123: 676–85.
30. Keyhani K, Miller III CC, Estrera AL, Wegryn T, Sheinbaum R, Safi HJ. Analysis of motor and somatosensory evoked potentials during thoracic and thoracoabdominal aortic aneurysm repair. *J Vasc Surg.* 2009;49(1):36–41.

30

Anesthesia for Esophageal Surgery

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Abbreviations

ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
COPD	Chronic obstructive pulmonary disease
CT	Computerized tomography
CXR	Chest X-ray (radiograph)
DLT	Double lumen endotracheal tube(s)
ECG	Electrocardiogram
EGD	Esophagogastroduodenoscopy
EUS	Endoscopic ultrasound
GDFT	Goal-directed fluid therapy
GERD	Gastroesophageal reflux disease
LEA	Lumbar epidural analgesia
LES	Lower esophageal sphincter
LVEDVI	Left ventricular end diastolic volume index
MIE	Minimally invasive esophagectomy
MRI	Magnetic resonance imaging
NGT	Nasogastric tube
OLV	One lung ventilation
PCA	Patient controlled analgesia
PEEP	Positive end expiratory pressure
PET	Positron emission tomography
PH	Paraesophageal hernia(s)
PONV	Postoperative nausea and vomiting
SLT	Single lumen endotracheal tube(s)
TEA	Thoracic epidural analgesia
TEF	Tracheoesophageal fistula
THE	Transhiatal esophagectomy
TTE	Transthoracic esophagectomy
UES	Upper esophageal sphincter

Key Points

- Patients presenting for esophageal surgery frequently have comorbidities including cardiopulmonary disease which should be evaluated per published ACC/AHA guidelines. Particular attention should be paid to symptoms and signs of esophageal obstruction, gastroesophageal reflux disease (GERD), and malnutrition which may affect the risk of perioperative complications.
- Postoperative pain control strategies are dictated by the surgical approach to the esophagus. Use of thoracic epidural analgesia in patients undergoing transthoracic esophageal surgery provides optimal pain control, permits early patient extubation and mobilization, and may improve outcomes.
- Patients presenting for esophageal surgery commonly have pathology which increases their risk of regurgitation and aspiration. This is particularly true for patients with achalasia and other motor disorders of the esophagus, patients with high-grade esophageal obstruction, and those with severe GERD. Consideration should be given to pharmacologic prophylaxis, awake or rapid sequence induction in a head-up position, and appropriate postoperative care, including gastric drainage.
- Excessive perioperative intravenous fluid administration, especially crystalloid, may lead to exaggerated fluid shifts toward the interstitial space causing increased complications such as poor wound healing, slower return of GI function, abdominal compartment syndrome, impaired anastomotic healing, increased cardiac demand, pneumonia, and respiratory failure. The ideal fluid regimen

for major esophageal surgery should be individualized, optimizing cardiac output and oxygen delivery while avoiding excessive fluid administration.

- Patients presenting for emergent repair of esophageal disruption, rupture or perforation may present with hypovolemia, sepsis, and shock. Anesthetic management strategies should be based on the severity of these presenting conditions and the nature of the planned procedure.
- Esophageal anastomotic leak is a frequent complication associated with high morbidity and mortality and is likely to be a function of numerous surgical, systemic, and possibly anesthetic factors. Since anastomotic integrity is dependent upon adequate blood flow and oxygen delivery, the development of anastomotic leak may be related to intraoperative management variables, particularly systemic blood pressure, cardiac output, and oxygen delivery and may thus be modifiable by anesthetic management.

Anatomy and Physiology of the Esophagus

The adult esophagus is a muscular tube, 18–26 cm in length, which acts as a conduit for the passage of food from the oral cavity into the stomach (Fig. 30.1). The esophagus begins at the level of the oropharynx; it then enters the superior mediastinum behind the trachea and left recurrent laryngeal nerve and passes into the posterior mediastinum behind the left mainstem bronchus. It continues caudad, passing posterior to the left atrium but anterior to the descending thoracic aorta. At the level of T10, the esophagus joins the stomach at the cardia after passing through the hiatus in the right diaphragm.

The upper esophagus is supplied by arterial branches of the superior and inferior thyroid arteries whereas the mid-esophagus receives its blood supply from the bronchial and right intercostal arteries as well as branches of the descending aorta. Distally, the esophagus is supplied by branches of the left gastric, left inferior phrenic and splenic arteries. Venous drainage from the upper segment is to the inferior thyroid veins, from the mid-segment to the azygous veins and from the lower esophageal segment to the gastric veins. The azygous and gastric veins form an anastomotic network between the portal and systemic venous systems and are thus the site of esophageal varices in patients with high portal pressure.

The esophagus receives innervation from both parasympathetic and sympathetic nerves. The parasympathetic input affects peristalsis via the vagus nerve, originating in the medulla, whereas both parasympathetic and sympathetic afferent nerves transmit information to the central nervous system via the spinal cord. Esophageal neuroanatomic pathways are shared by both the cardiac and respiratory systems, thus it may be difficult to ascertain which organ is responsible for chest pain syndromes.

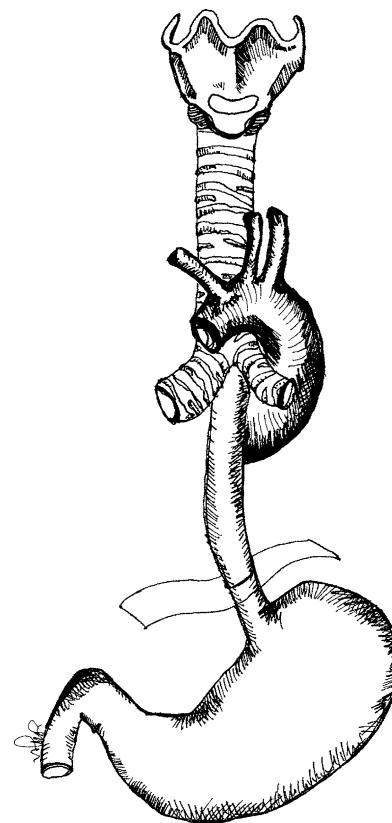


FIG. 30.1. Anatomic relationships between the esophagus, airway, aorta, diaphragm, and stomach.

Structurally, the esophagus is made up of four layers: the mucosa, submucosa, muscularis propria, and adventitia. The muscularis propria carries out most of the motor function of the esophagus. In the upper third of the esophagus, this muscularis propria is skeletal muscle but in the distal third it is smooth muscle, and the mid-section is mixed skeletal and smooth muscle. The upper esophageal sphincter (UES) is at the proximal origin of the esophagus where the inferior pharyngeal constrictor joins the cricopharyngeus muscle. UES tone is contracted at rest thus preventing aspiration of air during normal breathing. The lower esophageal sphincter (LES) is a 2–4 cm length of asymmetric circular smooth muscle within the diaphragmatic hiatus. At rest, the LES is contracted, preventing regurgitation of gastric contents. Swallowing elicits a wave of peristalsis which is under vagal control and carries a bolus of food from the pharynx to the stomach in 5–10 s. The coordinated relaxation of the LES allows the food bolus to enter the stomach.

A number of medications affect LES tone. Drugs known to decrease LES pressure include anticholinergics, sodium nitroprusside, dopamine, beta-adrenergic agonists, tricyclic antidepressant medications, and opioids. Drugs that have been found to increase LES tone include anticholinesterases, metoclopramide, prochlorperazine, and metoprolol.

Nonmalignant Disorders of the Esophagus and Surgical Therapies

Hiatal Hernia, Gastroesophageal Reflux Disease (GERD), and Esophageal Stricture

Gastroesophageal reflux and hiatal hernia may be present independently or may coexist. Esophageal strictures may be caused by a number of insults but are frequently related to gastroesophageal reflux. Gastroesophageal reflux is a common disorder and depending on diet and lifestyle, may affect up to 80% of the population. The term gastroesophageal reflux disease (GERD) applies when symptoms are more frequent or severe than the population norm. Pharmacotherapies including histamine blockers and proton pump inhibitors are widely used and may dramatically ameliorate symptoms and reduce the need for surgical therapy. Indications for surgery in patients with GERD include symptoms that are refractory to optimized medical therapy, esophageal stricture, pulmonary symptoms such as asthma and chronic cough, and severe erosive esophagitis.

GERD frequently coexists with hiatal hernia but many patients with a hiatal hernia remain asymptomatic. Hiatal hernias include the sliding hiatal hernia (type I) and paraesophageal hernias (PH) (types II, III, IV) (see Fig. 30.2a, b). Sliding hiatal hernias are most common and occur when the gastroesophageal junction and part of the fundus of the stomach herniate axially through the diaphragm into the thoracic cavity. Hiatal hernia is associated with a decrease in LES pressure [1] reducing barrier pressure between the esophagus and stomach, which in turn promotes reflux. PH occur when a portion of the stomach, typically the fundus, herniates into the thorax anterolateral to the distal esophagus (see Figs. 30.2b and 30.3). PH are much less common than type I hiatal hernias and

comprise approximately 5–15% of hiatal hernias [2]. PH are at risk of incarceration and the presence of a PH is thus considered an indication for surgical repair [3].

Surgical therapies for GERD and hiatal hernia can be achieved via a number of surgical incisions, but most commonly utilize a laparoscopic approach. Relative to laparotomy or transthoracic approaches, laparoscopic surgeries may produce considerably less pain, eliminate the need for a tube thoracostomy, utilize smaller incisions which decrease the risk of postoperative incisional hernias, and provide visualization for the diagnosis of other intra-abdominal pathology. A transthoracic approach may be preferred for patients with severe peptic strictures, patients requiring reoperation, and for those with other intrathoracic pathologies.

The transthoracic total fundoplication (Nissen) is performed through a left lateral thoracotomy (see Table 30.1 for a summary of thoracic esophageal procedures and anesthetic considerations). The distal esophagus and the esophagogastric junction are mobilized with preservation of the vagus nerve and exposure of the crura and left hepatic lobe. At the surgeon's request, the anesthesiologist places a 56–60 Fr esophageal dilator orally and advances it through the gastroesophageal junction. The proximal stomach is brought into the chest and a 2 cm fundoplication wrap is created with the fundus of the stomach. The dilator is removed and the fundoplication wrap placed below the diaphragm without tension. A nasogastric tube (NGT) and a chest drain are left in place postoperatively. Nissen fundoplication yields a high patient satisfaction rate (90–95%) when the procedure is performed by experienced surgeons [4, 5]. The transthoracic partial fundoplication (Belsey) is similar to the Nissen fundoplication but the esophageal wrap extends only 240–270° and is thus a partial fundoplication. The Belsey fundoplication yields a reduction

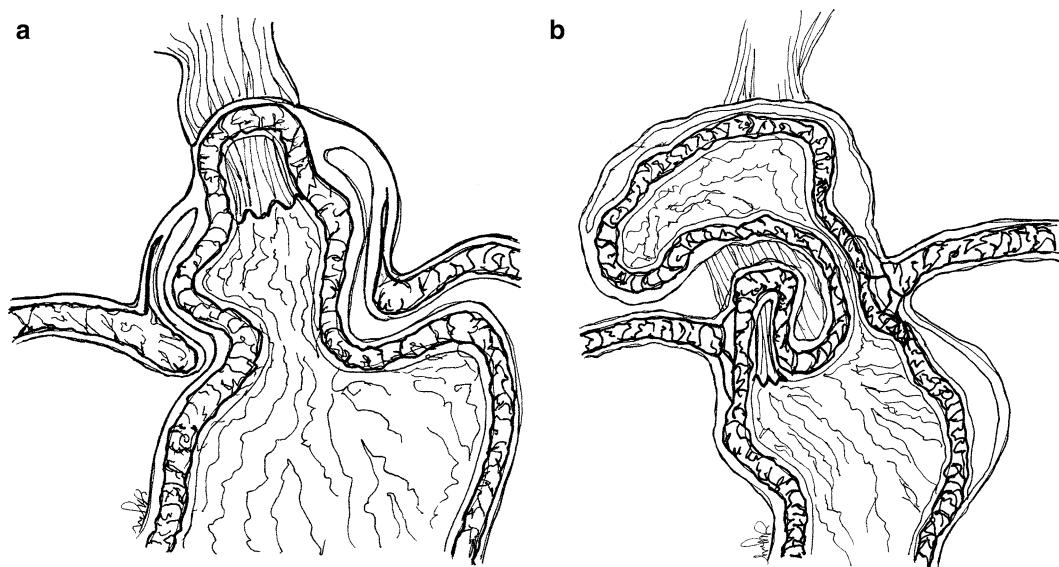


FIG. 30.2. (a) Type I hiatal hernia (sliding hernia). Note widening of the muscular hiatal orifice that allows cephalad herniation of the gastric cardia. (b) Type II hiatal hernia (paraesophageal hernia). The leading part of the herniating stomach is the fundus.

in GERD symptoms comparable to that of the Nissen and may cause fewer postoperative obstructive symptoms.

Chronic GERD can cause esophageal ulceration which leads to inflammation and may cause axial esophageal shortening and stricture formation. Medical therapy is inadequate for symptomatic stricture, though most can be internally dilated using any one of a number of dilating techniques. After dilation, surgical therapy aims to reduce reflux and prevent recurrence. The Collis gastroplasty, classically performed via a transthoracic approach, aims to lengthen the esophagus to facilitate a subsequent tension-free fundoplication. This procedure creates a tube of esophageal diameter from the lesser

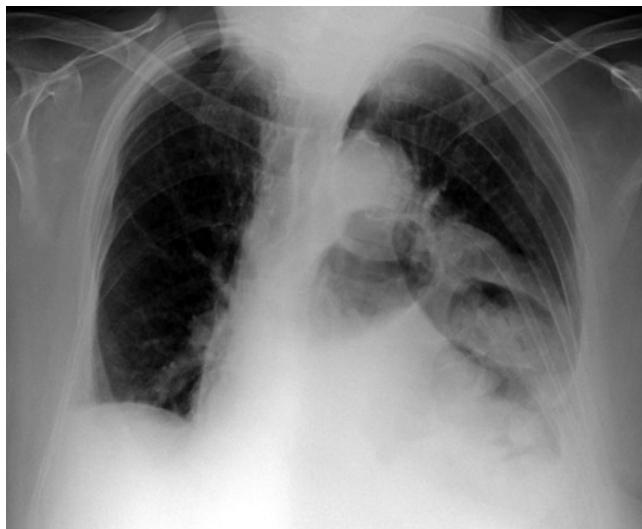


FIG. 30.3. Chest radiograph demonstrating a large left-sided type 4 paraesophageal hernia.

gastric curvature tissues via surgical stapling so that subsequent intra-abdominal fundoplication can be performed around the “neoesophagus.” In the context of advanced GERD with esophageal shortening, Collis gastroplasty combined with a fundoplication (Belsey) provided relief of GERD symptoms to 70% of treated patients overall, and to 89% who presented without dysphagia [6]. The Collis gastroplasty has also been used for the treatment of advanced GERD without esophageal shortening. Esophageal strictures that are not amenable to dilation may require esophagoplasty or esophagectomy.

PH can be repaired through a midline laparotomy, a laparoscopic approach, or via thoracotomy. At our institution, most large PH are repaired through a left thoracotomy. Through a thoracotomy incision the esophagus can be easily isolated and encircled, the hernia sac opened, its contents reduced to the abdomen, and the hiatus narrowed. Esophageal lengthening and fundoplication procedures are also frequently performed as part of the same procedure. Both transthoracic and laparoscopic approaches to the repair of PH are associated with good results, though recurrence rates remain a concern for both procedures [7, 8].

Esophageal Perforation and Rupture

Esophageal perforation typically occurs in the hospital and is often iatrogenic. Multiple etiologies of perforation exist including upper gastrointestinal endoscopy and the traumatic placement of esophageal dilators, NGTs, and misplaced endotracheal tubes. Perforation or disruption of the esophagus may also occur from external trauma, typically gunshot wounds or less commonly, from blunt trauma, from a foreign body, or chemical ingestion.

TABLE 30.1. Common transthoracic esophageal procedures and anesthetic considerations.

Surgical procedure	Surgical incision(s)/approach	Anesthetic considerations
Transthoracic total fundoplication (Nissen)	Left thoracotomy	Pain control
Transthoracic partial fundoplication (Belsey)		One lung ventilation
Collis gastroplasty		Aspiration risk
Thoracoscopic esophagomyotomy	Left thoracoscopy (4–5 ports)	Pain control
Heller myotomy and modified Heller myotomy	Left thoracotomy	One lung ventilation High aspiration risk Intraoperative esophagoscopy
Transhiatal esophagectomy	Midline laparotomy Left cervical Incision	Aspiration risk Risk of tracheobronchial injury, bleeding, cardiac compression, and dysrhythmias
Transthoracic esophagectomy (Ivor Lewis)	Midline laparotomy Right thoracotomy	Aspiration risk One lung ventilation
Three hole esophagectomy (McKewin)	Right thoracotomy Midline laparotomy Left cervical incision	Protective ventilation Fluid and hemodynamic management to optimize oxygen delivery Pain control Early extubation
Minimally invasive esophagectomy	Right thoracoscopy (4 ports) Laparoscopy (5 ports) Left cervical incision (variable)	Aspiration risk Protective ventilation Procedure duration

In contrast, esophageal rupture results from a sudden increase in intra-abdominal pressure with a relaxed LES and an obstructed esophageal orifice with vomiting, straining, weight lifting, childbirth, defecation, or blunt crush traumatic injuries to the abdomen and chest. Spontaneous rupture of the esophagus during vomiting is known as Boerhaave's syndrome. This rupture of the distal esophagus occurs under high pressure which forces gastric contents into the mediastinum and pleura [9].

Clinical presentation may be related to the mode of injury but is often nonspecific. Pain is the most common symptom [10], though fever, dyspnea, and crepitus also present not uncommonly. Mackler's triad, often associated with spontaneous esophageal rupture includes chest pain, vomiting, and subcutaneous emphysema. Soilage of the mediastinum elicits an inflammatory response that results in mediastinitis. Abdominal perforation may result in peritonitis. These patients may present with septic shock and are likely to deteriorate rapidly, particularly without aggressive resuscitation and definitive therapy.

Evaluation for esophageal perforation or rupture includes a plain film chest X-ray radiography (CXR) which may reveal mediastinal or free peritoneal air, pleural effusion, pneumothorax, widened mediastinum, and subcutaneous emphysema [11]. Computerized tomography (CT) scan will also confirm the rupture as evidenced by esophageal edema and thickening, possible abscess formation, as well as air and/or fluid in the pleural space. A water-soluble esophagogram will help to confirm the location and extent of the tear by allowing visualization of the extravasation of contrast.

Treatment of esophageal rupture or perforation depends mainly on the extent and location of the tear and the disease state of the esophagus. The time interval between injury and repair may also play a role in determining the appropriate strategy for treatment. Perforation of the cervical esophagus may be treated solely by drainage; surgical repair is preferred for thoracic or abdominal esophageal perforations. In a stable patient without severe esophageal pathology, primary closure of a thoracic or abdominal esophageal perforation can be attempted. If the area of injury is diseased, an esophagectomy may be required. Early aggressive surgical treatment of Boerhaave's syndrome is favored; left untreated this condition is virtually always fatal [9]. Conservative nonoperative therapies emphasizing aggressive drainage of fluid collections and appropriate antibiotic therapy are preferred by some clinicians for stable patients with contained esophageal leaks [12] and may be associated with acceptably low morbidity and mortality [12, 13]. Case reports and small case series have also demonstrated the efficacy of treating esophageal perforation and esophageal anastomotic leaks with self-expandable plastic and metallic stents [14–16].

Achalasia and Motility Disorders

Achalasia is a disease of impaired esophageal motility, most often affecting the distal esophagus. It affects approximately

1 in 100,000 persons per year, with an equal gender distribution [17]. The etiology of achalasia is unknown but characteristic features include increased LES pressure, incomplete relaxation of the LES with swallowing and loss of peristalsis which causes impaired esophageal emptying. Primary achalasia is due to a complete loss or relative absence of ganglion cells in the myenteric plexus. This causes an imbalance between excitatory and inhibitory neurons which results in impaired relaxation of the LES [18]. Other primary motor disorders of the esophagus include nutcracker esophagus and diffuse esophageal spasm. Secondary achalasia is most often caused by Chagas' disease, a systemic disease due to infection with *Trypanosoma cruzi* [19]. Other secondary motor disorders are associated with systemic disease processes such as scleroderma, diabetes, amyloidosis, Parkinson's disease, and neuromuscular diseases of skeletal muscle.

Achalasia progresses slowly and thus when patients finally present for treatment they are often at advanced stages of the disease. Symptoms of achalasia include dysphagia, first for solids and then liquids. As the esophagus dilates, regurgitation becomes a more frequent problem. Patients may describe chest pain due to esophageal spasm. Weight loss, symptoms of GERD, history suggestive for aspiration such as pneumonia and chronic cough are also consistent with achalasia [20].

Radiographic findings in advanced achalasia include absence of gastric bubble, esophageal dilation, and fluid filling [21]. Barium swallow reveals the esophageal air-fluid level and a characteristic bird's beak narrowing caused by the impaired relaxation of the LES [21] (see Fig. 30.4).



FIG. 30.4. This thoracic level barium swallow esophagogram illustrates a classic radiologic feature of achalasia – bird-beak appearance of the esophagus.

Esophageal manometry is a sensitive diagnostic test for achalasia and manifestations include elevated LES resting pressure and incomplete relaxation of the LES, aperistalsis of the esophageal body, and elevated lower esophageal baseline pressure [20]. Treatment goals for achalasia include elimination of the esophageal outflow obstruction due to the tight LES, alleviating dysphagia and minimizing gastroesophageal reflux [20]. Nonsurgical treatments include calcium channel blockers and nitrates, botulinum toxin injection, and balloon dilatation of the LES. The superiority of surgical myotomy with fundoplication is supported by a recent systematic review and meta-analysis [22].

Laparoscopic esophagomyotomy is performed with the patient in modified lithotomy, reverse Trendelenberg position and includes an anterior longitudinal myotomy of the distal esophagus, esophagogastric junction, and proximal stomach. Thoracoscopic esophagomyotomy is performed through a thoracoscope via the left chest which allows for optimal visualization of the lower esophagus and cardioesophageal junction [23, 24]. The Heller and modified Heller myotomy procedures are performed via a left thoracotomy incision and differ in the extent of the myotomy incision and the inclusion of a fundoplication to minimize reflux. The Heller procedure utilizes a shorter myotomy incision extended only 1 cm or less onto the stomach. The modified Heller myotomy includes a 10 cm myotomy incision and a partial anterior gastric fundoplication to decrease the risk of reflux postoperatively [24].

Minimally invasive laparoscopic and thoracoscopic Heller and modified Heller myotomy procedures have been shown to be safe, effective, and durable treatments for achalasia [25–37]. Patient outcomes after minimally invasive myotomy surgery for achalasia generally favor the laparoscopic approaches, however. Multiple investigators have found that patients experience superior dysphagia relief and less postoperative reflux with the laparoscopic approach as compared to the thoracoscopic approach [25, 28, 32, 33]. This difference may result from the limitations in extending the myotomy incision into the stomach and creating a fundoplication wrap from the thoracoscopic approach.

Tracheoesophageal Fistula (TEF)

Tracheoesophageal fistula (TEF) in adult patients is most commonly a result of malignancy, though TEF after traumatic injury [38] and intubation or tracheostomy [38–42] is also described. Though less common, TEF of congenital origins has also been reported [43–45]. Rarely, the diagnosis of TEF may be made intraoperatively [46], in the perioperative period [43, 47], or in chronically intubated patients [40–42].

TEF can be managed by either surgical or nonsurgical means, depending largely on the etiology. Nonoperative management of TEF with malignant etiology is generally favored as the presence of a TEF in association with malignancy generally indicates nonrespectability. Placement of an esophageal stent may provide suitable palliation [48] and survival is related to tumor biology rather than the fistula itself [48].

In critically ill patients dependent on mechanical ventilation, the use of esophageal stents to provide temporary closure of benign TEF was a safe and effective procedure for palliation [49]. The treatment of postintubation TEF is more aggressive and tracheal or laryngotracheal resection with primary closure of the esophagus has been recommended [50].

Esophageal Diverticula

Esophageal diverticula are classified according to their anatomic location (cervical or thoracic) and pathophysiology (pseudo- or traction diverticula). Most diverticula are acquired and occur in an elderly patient population. Pulsion or pseudodiverticula are the most common form and consist of a localized outpouching which lacks a muscular covering; that is, the wall consists of only mucosa and submucosa herniating through the muscle layer. Most pseudodiverticuli are of the Zenker's variety, located in the hypopharynx. Epiphrenic diverticula are located within the thoracic esophagus, typically in the distal esophagus [51]. True or traction diverticula occur within the middle one third of the thoracic esophagus as a result of paraesophageal granulomatous mediastinal lymphadenitis usually due to tuberculosis or histoplasmosis and are characterized by full-thickness involvement of the esophageal wall. These diverticula are typically small and most are asymptomatic. Complications are uncommon but may include TEF formation.

Clinical presentation of Zenker's diverticulum usually includes dysphagia for solid food and regurgitation of undigested food substances. Patients may also complain of halitosis, gurgling associated with swallowing, and symptoms associated with aspiration such as nighttime cough, hoarseness of voice, bronchospasm, and chronic respiratory infection. Diagnostic confirmation is accomplished with barium contrast study which clearly demonstrates the diverticulum.

Surgical correction of Zenker's diverticulum is usually accomplished via a left cervical incision and includes a cricopharyngeal myotomy. While the myotomy may be sufficient therapy for small diverticula, larger sacs require diverticulectomy or diverticulopexy [51, 52]. Minimally invasive techniques used to treat Zenker's diverticulum have included endoscopic stapling diverticulostomy, fiberoptic endoscopic electrocautery, and laser coagulation techniques [51–54]. In general, minimally invasive treatments for Zenker's diverticulum have yielded satisfactory results in the majority of patients [54, 55] and most can be performed in an endoscopy unit with a brief general anesthetic or in an awake patient.

Thoracic esophageal diverticula are usually epiphrenic and most are found to be associated with an esophageal motor disorder such as achalasia. While many patients do not have symptoms specifically referable to the diverticulum, if present these may be difficult to distinguish from those of the associated motor disorder. Patients who are asymptomatic or present with mild symptoms are not surgical candidates. Presenting symptoms may include dysphagia, chest pain, regurgitation of ingested foods, and symptoms of aspiration. Patients with epiphrenic diverticula are advised to undergo both barium



FIG. 30.5. A thoracic level barium swallow esophagogram which demonstrates a large mid-esophageal diverticulum filled with contrast.

swallow examination (see Fig. 30.5 for barium esophagogram of a mid-esophageal diverticulum) and esophageal manometry to delineate any associated pathology such as motility disorder, malignancy, or stricture. Patients with incapacitating symptom profiles are referred for surgery.

Surgical goals include resection of the diverticulum and usually, a myotomy to treat the accompanying motor disorder, with or without an antireflux procedure. The classical surgical approach has been through a left thoracotomy incision, through which the diverticulum is dissected and excised; a myotomy and a fundoplication may also be performed. Results of surgical therapy are favorable, completely eliminating symptoms in 74% of patients [56]. Thoracoscopic and laparoscopic approaches have also been described but the number performed is relatively low, commensurate with the rarity of these lesions.

Malignant Disease of the Esophagus and Esophagectomy

Esophageal Cancer

Malignant esophageal tumors can be classified on the basis of histologic types – squamous cell carcinoma and adenocarcinoma, which differ with respect to affected populations,

incidence, etiology, and risk factors. While squamous cell carcinoma still accounts for the vast majority of esophageal cancers worldwide, the incidence of adenocarcinoma has risen sharply throughout the Western world, now accounting for nearly half of esophageal cancers in many countries [57, 58]. Potential etiologic and predisposing factors identified through epidemiologic study include tobacco use and excessive alcohol ingestion, gastroesophageal reflux, obesity, achalasia, and low socioeconomic status [57].

Clinical presentation of patients with esophageal cancer is variable; patients may present with symptoms of dysphagia, odynophagia, and progressive weight loss. Patient evaluation should include a thorough history and physical examination with attention to local tumor effects, possible sites of metastasis, and general health. Clinical investigations include the barium contrast swallow study to define esophageal anatomy and esophagogastroduodenoscopy to permit biopsy and definitive identification of tumor type. Both CT scans and magnetic resonance imaging (MRI) are used clinically for noninvasive staging of esophageal cancer. Endoscopic ultrasound (EUS) has been used for imaging of local/regional esophageal disease and may be considered complementary to CT scanning. Positron emission tomography (PET) is being used with greater frequency for the purpose of staging esophageal cancer and for assessing the response to induction chemotherapy.

In an effort to avoid the morbidity, mortality, and expense associated with esophagectomy, many centers are employing relatively new approaches to esophageal preservation in patients with malignant and premalignant esophageal lesions. The close surveillance of many patients with premalignant disease of the esophagus has led to the early identification of many cases of high-grade dysplasia and superficial adenocarcinoma. Advances in the use of minimally invasive endoscopic techniques permit the staging of superficial esophageal cancers by endoscopic biopsy [59, 60] and where appropriate, endoscopic resection of adenocarcinoma limited to the esophageal mucosa [61, 62].

Unfortunately, patients often present with advanced local/regional and metastatic disease. The failure of surgery to cure most advanced local and regional disease and the early systemic dissemination of esophageal cancers has led to significant interest in improving chemotherapeutic regimens. Chemotherapies are now routinely used in the context of esophageal cancer both for palliation of locally advanced and metastatic disease and increasingly as an adjunct to surgical resection. 5-Fluorouracil and cisplatin are widely used in combination preoperative therapy for both adenocarcinoma and squamous cell carcinoma of the esophagus [63]. Combination therapy may improve survival but appears to also increase the risk of serious therapy-associated complications [64]. Neoadjuvant chemotherapy with or without radiotherapy is widely used and is believed to improve curative resection rate, though survival differences have been difficult to demonstrate in small studies. A recent review of meta-analyses investigating neoadjuvant chemotherapy with radiation suggests an improved pathologic response which may improve survival but also underscores the need for additional high quality clinical trials to confirm these findings [65].

Esophagectomy

Esophagectomy is indicated for the resection of esophageal cancer without local invasion or metastasis [66], curative resection of high-grade dysplasia [67], and may also be used for severe nonmalignant disorders including esophageal injury, nondilatable stricture, severe recurrent GERD, and achalasia [68, 69]. Esophagectomy surgery can be performed via a transhiatal approach by laparotomy, a two incision surgery utilizing both laparotomy and right thoracotomy (Ivor Lewis), a three incision approach (McKewin) which also requires a cervical incision for anastomosis, and minimally invasive approaches utilizing laparoscopy and/or thoracoscopy (see Table 30.1). Consideration for the transhiatal, transthoracic, and minimally invasive esophagectomy (MIE) will be discussed later.

Transhiatal esophagectomy (THE) is performed for tumors throughout the esophagus but is often preferred for lower tumors. The primary advantage of this resection is that it avoids a thoracotomy and the possibility of an intrathoracic anastomotic leak. This procedure is accomplished via a large upper abdominal incision which is used to mobilize the stomach and through which transhiatal esophageal dissection is carried out and a cervical incision through which the conduit is introduced and the anastomosis is made. The transhiatal approach to esophagectomy requires the manual dissection of the esophagus from the mediastinum blindly via the abdominal hiatus.

There continues to be considerable debate regarding the relative risk of THE relative to the transthoracic esophagectomy (TTE) procedure, both from a surgical and oncologic standpoint. While the morbidity and mortality associated with THE have declined over the past several decades [70], the advantage of THE over TTE remains controversial with both early morbidity and mortality advantages demonstrated [71, 72] and refuted [73]. It is also not clear whether surgical approach affects long-term survival; a meta-analysis of multiple comparative studies demonstrated equivalent (20%) 5-year survival in both groups [71], though a trend towards an improved survival in the TTE group has also been reported [72].

The transthoracic approach to esophagectomy is performed for malignant, premalignant, or nonmalignant disease of the esophagus and employs an abdominal incision for mobilization of the stomach and formation of a gastric tube or other esophageal conduit and a right thoracotomy through which the diseased esophageal portion is resected and the anastomosis is made. The TTE is often preferred when the resection extends to other mediastinal structures, mediastinal fibrosis is known or suspected, tumor may involve the airway or vascular structures, or an intrathoracic anastomosis is required.

The term “minimally invasive esophagectomy” (MIE) encompasses a variety of surgical approaches to esophagectomy that attempt to minimize the degree of surgical trespass in one or more body cavities. True MIE using laparoscopy and thoracoscopy is performed in very few centers. Analogous to the open procedures, several variants are possible; the most popular are the minimally invasive equivalents of the Ivor Lewis and three hole esophagectomies. Thus far, outcome data are limited, but encouraging. In a clinical series of 222 MIE cases, morbidity and mortality outcomes compared favorably to those of open esophagectomy [74]. Randomized trials directly comparing MIE with open esophagectomy will be required before definitive benefits can be declared, but it is conceivable that advantages with regard to pain control, respiratory complications, length of stay, total cost, and quality of life may yet be demonstrated.

Esophageal Conduits

Although a variety of conduits have been used after esophageal resection, stomach is usually preferred because of its excellent blood supply, because it can be readily mobilized to reach the thorax or neck, and because only one anastomosis is required. However, the stomach may not be a suitable conduit in the case of prior gastric surgery or tumor involvement. In such cases, an alternative conduit must be used. The pedicled colonic interposition utilizes a segment of colon with an attached vascular pedicle as an esophageal replacement conduit. While the pedicled colon graft has adequate mobility its use is associated with numerous complications including conduit redundancy and symptoms related to inadequate food transit [75–79] which may impact quality of life [76] and long-term outcomes [80]. Additionally, atherosclerotic disease may affect vascular supply to the colon which may in turn increase the risk of colonic ischemia and necrosis, a major cause of morbidity and mortality [81–83].

Jejunum has a number of theoretical advantages over that of colon for use as an esophageal replacement. First, its diameter more closely approximates that of the esophagus. Secondly, it is generally disease free. Additionally, its intrinsic peristaltic activity may improve food transit and reduce symptoms postoperatively [84–88]. Use of the jejunum for interposition has previously been limited by the vascular anatomy of the jejunum. The jejunal mesentery lacks the collateral arcades of the colon which permit them to reach interposition sites in the thorax and neck. Ischemia of the interposition graft is the likely cause of jejunal loop gangrene which plagued early attempts and led to an interest in vascular augmentation of the interposition graft, now known as “supercharging.”

Recent advances in microvascular surgery have enabled specialized centers to expand the indications for jejunal interposition beyond short-segment esophageal replacement. Esophagectomy with “supercharged” jejunal interposition graft is undertaken as a one-stage procedure which includes esophageal resection, construction of the interposition graft with esophageal and jejunal reconstruction. The superior jejunal vascular arcade is “supercharged” by reimplantation into cervical or internal mammary arteries. The inferior arcade retains its native supply from the superior mesenteric artery. A recent series utilizing this supercharging technique

for construction of jejunal interposition grafts for esophageal reconstruction demonstrated a 92% success rate for discharge with an intact flap. Ninety-five percent of patients were discharged on a regular diet and without reflux symptoms [89, 90]. Despite some successes, this technique remains the purview of highly specialized centers with multidisciplinary teams and is considered only in the absence of a suitable gastric conduit.

Anesthetic Management of Esophageal Surgery Patients

Preoperative Evaluation and Preparation

A thorough history and physical examination should be performed prior to anesthetizing a patient for esophageal surgery. Comorbid conditions should be evaluated and optimized prior to surgery. Particular attention should be given to signs and symptoms of esophageal obstruction, GERD, and silent aspiration. Symptoms of obstruction, particularly dysphagia and odynophagia, may lead to reduced oral intake and malnutrition which can lead to increased morbidity and mortality [91, 92]. Symptoms of severe GERD with aspiration may include water brash (hypersalivation in response to reflux), coughing when supine, globus sensation (feeling of lump in throat), laryngitis, and asthma-type symptoms.

The presence of significant cardiovascular disease has important implications for patients undergoing major surgical procedures involving the esophagus. Patients may be evaluated for cardiovascular risk with attention to the ACC/AHA guidelines for perioperative cardiovascular evaluation [93]. The risk of cardiovascular complications during major surgical procedures of the esophagus may be increased by a number of factors inherent to surgery and anesthesia care, including the degree of planned physiologic trespass, hypoxemia, hemorrhage, dysrhythmias, and pain. One lung ventilation (OLV) is often required for surgery of the esophagus. Oxygenation, ventilation, and weaning from mechanical ventilation may be more difficult in the patient with pulmonary disease. The minimum preoperative evaluation of the cardiopulmonary system should include a twelve-lead electrocardiogram (ECG) and CXR. A preoperative ECG serves as a screening test for myocardial ischemia and arrhythmias and provides a baseline for comparison in the event of perioperative cardiac complications. Preoperative CXR may reveal evidence of aspiration as well as coexisting pulmonary and cardiac disease. Patients with a history of morbid obesity or chronic lung disease should also undergo preoperative pulmonary function testing if the procedure involves a thoracotomy approach.

Patients with severe GERD or those otherwise at risk for aspiration pneumonitis may benefit from prophylactic medication to increase gastric pH and decrease gastric volume. Though definitive evidence of risk reduction is lacking, appropriate pharmacologic prophylaxis with H_2 receptor antagonists

or proton pump inhibitors is known to reduce gastric volume and acidity [94–99] and is thus likely to reduce the incidence and severity of pneumonitis should aspiration occur.

Patients may present for esophagectomy surgery after having received neoadjuvant chemotherapy which may improve survival [63, 65]. The chemotherapeutic agents used to treat esophageal cancer cause bone marrow suppression and patients often present with some degree of anemia and thrombocytopenia. The need for optimizing patient status prior to major surgery should be balanced with the risk of delaying the resection of malignant tumors. Occasionally, severe thrombocytopenia may preclude the preoperative placement of an epidural catheter in which case alternative plans for analgesia should be made.

Intraoperative Monitoring

In general, intraoperative monitoring for esophageal surgery cases should be commensurate with the degree of physiologic trespass inherent in the planned procedure and the nature and severity of patient comorbidity. Routine monitoring should include pulse oximetry, noninvasive blood pressure monitoring, and electrocardiography. Since many patients presenting for esophageal surgery have comorbid disease of the cardiovascular and respiratory systems, consideration should be given to invasive monitors where appropriate. With the exception of patients with advanced cardiovascular or pulmonary disease, routine intraoperative monitors will generally suffice for those patients presenting for endoscopic and minimally invasive procedures limited to the abdominal cavity. Transthoracic approaches to the esophagus generally mandate a more aggressive approach to monitoring. An indwelling arterial catheter for continuous measurement of systemic arterial blood pressure is the standard of care for these procedures. Surgical manipulation of thoracic and mediastinal structures can profoundly affect determinants of cardiac performance including venous return and cardiac filling and may contribute to the development of dysrhythmias, all of which can compromise cardiac output and hemodynamic status. In addition, many of these procedures require lung isolation and OLV, a ventilation strategy which substantially limits arterial oxygenation. Surgical dissection can lead to unexpected bleeding, occasionally massive in nature. Point of care testing of arterial blood samples can aid in the assessment and maintenance of adequate arterial oxygenation, acid base status, as well as hemoglobin and electrolyte concentrations.

In the patient with normal cardiovascular reserve, central venous access is not generally necessary and does not provide useful information for volume management. Nonetheless, central access may be required in patients with very limited peripheral venous access, especially obese patients in whom it may be difficult to re-establish lost venous access intraoperatively, patients requiring emergency surgery for esophageal trauma or perforation as septic complications can rapidly ensue, and those patients who are likely to require vasopressor

or inotropic support. Patients undergoing esophageal surgery should also undergo bladder catheterization for decompression and for the monitoring of urine output. Temperature monitoring is easily accomplished via a probe in the oropharynx, axilla, or bladder catheter. Euthermia can be achieved by use of commercially available forced warm air heating blankets and fluid warmers.

Pain Control

Pain control after esophageal surgery is dictated largely by the surgical approach to the esophagus. Most patients undergoing endoscopic surgery of the esophagus have little pain postoperatively and thus do not require an aggressive plan for analgesia. Similarly, a laparoscopic approach is generally not associated with high analgesic requirement postoperatively. However, the thoracotomy incision utilized in most transthoracic esophageal surgeries is one of the most painful surgical incisions in common use. As such, anesthetic techniques for postoperative pain control play an extremely important role in optimizing outcomes after transthoracic esophageal procedures. Although a variety of pain control approaches have been utilized, most centers favor the use of thoracic epidural analgesia (TEA) for its excellent analgesia [100, 101], favorable safety profile, cost savings [102, 103], its potential role in improving outcomes after transthoracic esophageal surgery [103–107], and as a component in multimodal strategies to expedite patient mobilization and recovery after esophagectomy [108–111].

In comparison to parenteral opioid pain therapy alone, TEA provides superior analgesia after esophagectomy [100, 101] and is considered by many surgeons and anesthesiologists to represent the “gold standard” with regard to postoperative pain control after thoracotomy in general. However, for technical and safety reasons, not all patients are suitable candidates for the placement of thoracic epidural catheters. For patients in whom TEA is not possible but epidural analgesia per se is not contraindicated, lumbar epidural analgesia (LEA) may represent a compromise approach for analgesia after thoracoabdominal esophagectomy though pain control postoperatively is inferior to that obtained by TEA [112].

A variety of nonneuraxial techniques have been studied and recommended for postthoracotomy pain control; the most promising of these include intrapleural, intercostal, and paravertebral approaches. Intercostal nerve catheters in combination with patient controlled analgesia (PCA) have been compared with TEA producing mixed results [113, 114]. Intrapleural and thoracotomy wound catheters have also been utilized, though rigorous comparison to standard therapies are lacking [115, 116]. Paravertebral blockade has shown promise as an alternative therapy [117] with analgesic efficacy comparable to that of TEA by randomized trial [118] and meta-analysis [119] and with a favorable side-effect profile [119] and has been advocated as a superior modality by several authors [120, 121]. Whether paravertebral analgesia will

replace TEA for postthoracotomy pain may depend on the identification of outcome advantages that have thus far been ascribed only to TEA.

Specific epidural management strategies should ideally consider the dermatomal range of incision(s), the impact of incisional pain on respiratory function, the likelihood and impact of respiratory depression, and the intraoperative impact of an epidural induced sympathectomy on hemodynamic status. Since the thoracoabdominal esophagectomy requires both thoracotomy and laparotomy incisions, any plan for postoperative pain control should address this fact. A variety of management strategies have been reported, but most centers which perform transthoracic and thoracoabdominal esophageal surgeries utilize a multimodal approach to pain management including preoperative placement of a thoracic epidural catheter unless contraindicated, intra- or postoperative bolus and infusion of a dilute local anesthetic such as ropivacaine or bupivacaine along with fentanyl or hydromorphone. An additional epidural bolus of preservative free morphine may provide a wider neuraxial spread and may provide synergism with the infused local anesthetics, but requires postoperative respiratory monitoring because of the possibility of delayed respiratory depression. Whether to bolus or infuse epidural local anesthetics pre- or intraoperatively has been a subject of debate among anesthesiologists. Arguments that a preemptive initiation of analgesia might provide better acute and chronic pain control have been based largely on theoretical considerations. Results thus far are mixed, suggesting that preoperative dosing of epidural catheters may produce better acute pain control [122, 123]. Although acute pain after thoracotomy has been shown to predict chronic pain [124], the efficacy of preemptive epidural analgesia on preventing chronic postthoracotomy pain is not supported by a recent meta-analysis [123].

Induction and Airway Management

Induction of general anesthesia and airway management in patients undergoing esophageal surgery is dictated largely by patient factors including cardiopulmonary status, hemodynamic and nutritional status at the time of induction, mediastinal mass effect if any, perceived risk of aspiration pneumonitis, and procedural factors including anticipated length of and nature of the procedure (i.e., if OLV is required for an intrathoracic procedure). Patients presenting for emergency procedures of the esophagus and stomach may lack the desired preoperative evaluation of cardiopulmonary status and can present with unstable hemodynamic or pulmonary status from a variety of factors including underlying cardiopulmonary disease, aspiration, sepsis, acute respiratory distress syndrome (ARDS), or hemorrhage. Most practitioners favor intravenous induction agents such as propofol, thiopental, etomidate, or ketamine in conjunction with a rapidly acting neuromuscular blocking agent such as succinylcholine or rocuronium to facilitate smooth induction of anesthesia and rapid tracheal intubation.

Patients presenting for elective esophageal procedures will be stable at induction but complications arising from the presence of a mediastinal mass may accompany the induction of anesthesia, positive pressure ventilation, and muscle relaxation. Tracheobronchial compression or obstruction and cardiovascular collapse associated with anesthetic induction in patients with anterior mediastinal masses have been well described and is discussed in Chap. 14. Airway compromise has also been reported spontaneously or during the conduct of anesthesia in patients with posterior [125–129] and superior [130–132] mediastinal masses. Posterior mediastinal masses, including those of esophageal origin [125–127] and the dilated esophagus itself [133] may impinge on the airway and cause obstruction. The trachea is most easily compressed posteriorly because of the lack of cartilaginous support, and thus posterior compression can result in near complete expiratory obstruction [129]. The identification of patients with mediastinal masses who are at risk for cardiopulmonary complications is imprecise but specific factors associated with increased risk have been reported [134] and may aid in management.

Anesthetic management of patients for esophageal surgery presents an additional challenge with regard to the perceived risk of aspiration. Patients in need of esophageal surgery are widely considered to be at elevated risk of aspiration and its sequelae [135–138] (see Fig. 30.6) and the use of rapid sequence induction techniques are widely used and advocated [136, 137]. Those patients with severe gastroesophageal pathology, particularly those with obstructive disease and dysmotility syndromes may represent high-risk subgroups but clear risk stratification is lacking. Achalasia, in particular, has been asso-

ciated with spontaneous aspiration pneumonitis [139, 140] and these patients may benefit from longer periods of NPO status. Practice guidelines for preoperative fasting have been published [141] and effect of fasting regimens has been reviewed [142] but apply to healthy patients undergoing elective surgical procedures. Optimal periods of NPO status in patients with severe gastroesophageal pathology are not known.

Rapid sequence induction and intubation has been widely advocated in patients thought to be at elevated risk of regurgitation and aspiration. This technique has classically referred to the rapid intravenous administration of induction agent and muscle relaxant, accompanied by the application of cricoid pressure (Sellick maneuver) and immediate laryngoscopy and tracheal intubation without intervening positive pressure ventilation. The rationale underlying this approach is that (1) the cricoid cartilage is positioned anterior to the esophagus, (2) that downward pressure on the cricoid cartilage on a patient in the supine position would be transmitted to the esophagus, occluding the esophageal lumen by compressing it against the adjacent vertebral body, and (3) that this compression would result in a clinically significant effect on passive regurgitation, and thus aspiration in the anesthetized patient. Arguably, rapid sequence induction with cricoid pressure has represented the standard of care for patients at risk for pulmonary aspiration in many centers. There is currently, however, considerable controversy regarding the efficacy and safety of this maneuver [143, 144]. There is also a growing awareness that the assumptions underlying the use of cricoid pressure and the efficacy of cricoid pressure in preventing regurgitation and aspiration remain unproven. Pressure applied to the cricoid cartilage increases the lateral displacement of the esophagus without reliably compressing it [145]. Though a recent study has shown that cricoid pressure compresses the hypopharynx, decreasing its diameter by 35%, it is not known whether this is sufficient to obliterate the lumen [146]. Cricoid pressure also displaces and compresses the airway [145], potentially increasing the difficulty associated with airway management [147, 148], and is contraindicated in the context of known or suspected cricoid or tracheal injury, unstable cervical spine, and during active vomiting. Additionally, cricoid pressure is not without risk, having been associated with fracture of the cartilage [149] and a variety of other risks [147, 148, 150]. It is also worth noting that cricoid pressure is associated with a decrease in LES pressure and esophageal barrier pressure [151] which could increase the risk of passive regurgitation in the anesthetized patient. This is consistent with the well-described phenomenon of regurgitation and aspiration during the application of cricoid pressure [135, 152, 153]. Finally, reviews of the available evidence regarding the efficacy of cricoid pressure in preventing aspiration in the context of rapid sequence induction fail to support the notion that it decreases the risk of aspiration [148, 154]. Since our current understanding of aspiration and the protective effects of cricoid pressure, if any, are incomplete, the decision to apply cricoid pressure in the context of a rapid sequence induction

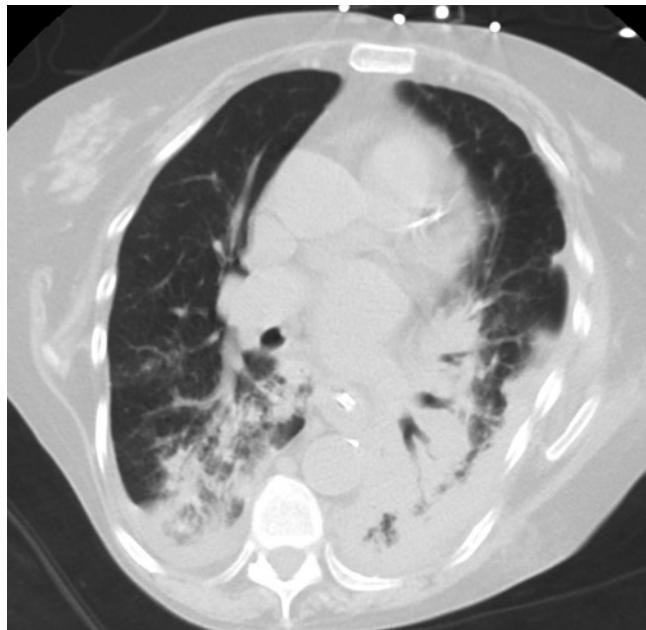


FIG. 30.6. CT scan of the thorax which demonstrates multifocal bibasilar consolidations consistent with the patient's history of aspiration pneumonitis.

should be individualized and based on an understanding of the relevant anatomic and physiologic principles and the specific clinical context.

Though there is little definitive evidence with regard to practical aspects of aspiration pneumonitis risk reduction to guide the practitioner, we suggest the following approach. If there is any anatomic or historical evidence to suggest a difficult intubation, serious consideration should be given to intubation in the awake patient, particularly for patients at highest risk of aspiration – those presenting with achalasia, high-grade esophageal obstruction and those requiring emergency procedures with full stomachs. For those patients with airways judged to be easily manageable, the use of a rapid sequence induction is prudent. Minimizing the time between loss of consciousness, muscle relaxation, and tracheal intubation with a lubricated cuffed tube is likely to reduce risk. It is also worth considering the possible effect of patient position on aspiration risk. A head-up or reverse Trendelenberg position may reduce the passive reflux of gastric contents and aspiration risk [155–157] in addition to the known benefits of this position on pulmonary mechanics, particularly in the obese patient and has been previously advocated [135, 155].

The suggestion that aspiration of gastric contents may be a contributing factor in the development of pulmonary complications in thoracic surgery patients is derived, in part, from evidence of intraoperative tracheal aspiration in intubated patients undergoing thoracotomy [158]. In this study, premedication with ranitidine decreased the incidence of measured gastric acid regurgitation but effects on reduction of tracheal acid aspiration were not statistically significant. Clearly, acid aspiration in patients intubated with double lumen endotracheal tubes (DLT) is possible [158] though dye studies suggest that gel lubrication of the tube cuff may reduce leakage and aspiration [159, 160]. Other strategies to minimize the risk of tracheal aspiration in patients undergoing esophageal surgery include appropriate preoperative suctioning of the NGT if present, and of the NGT and oropharynx prior to tracheal extubation. A low level of continuous suctioning of the NGT after major esophageal surgery may also help reduce the incidence of subacute and chronic aspiration postoperatively [161].

Intraoperative Management

After the induction of general anesthesia and tracheal intubation, the maintenance of anesthesia can be accomplished by a variety of approaches, though many authors prefer a balanced anesthetic technique with the use of a volatile inhalational agent such as isoflurane, sevoflurane or desflurane, a nondepolarizing paralytic agent, intravenous opioids, and opioids and/or local anesthetic agents via an epidural catheter if present [109, 111]. As volatile anesthetic agents are known to precondition the myocardium against subsequent ischemic insult, there is a theoretical advantage in the use of these agents. Given the overlap of risk factors for coronary disease

and esophageal disease, patients presenting with surgical esophageal disease may also be at risk for myocardial ischemia and thus may benefit from such protection, though clinical evidence of benefit in this population is lacking. A total intravenous anesthetic with propofol infusion is also a viable option, though this technique lacks the theoretical advantage of myocardial preconditioning and is likely to be significantly more expensive, particularly for longer surgeries.

Lung Isolation and One Lung Ventilation

Surgical approaches to the thoracic esophagus have been greatly facilitated by the development of techniques for lung isolation and OLV. In most major centers, lung isolation and OLV are considered the standard of care for transthoracic approaches to the esophagus and are essential for thoracoscopic esophageal surgery. The most commonly utilized modalities are DLT and endobronchial blockers. Left-sided DLT are most commonly employed for transthoracic esophageal surgery and they have the advantage of being easily placed by experienced practitioners, providing excellent lung isolation and operating conditions while providing access to both lungs for suctioning, ventilation, and oxygen administration. Additionally, because the left mainstem bronchus is longer than that of the right, positioning is more easily accomplished without compromising left upper lobe ventilation.

However, the use of a DLT may be relatively or absolutely contraindicated in some patients or may be difficult to achieve, necessitating another approach. First, endotracheal intubation with a DLT may require more time than with a single lumen tube [162]. This may increase the risk of aspiration in the high-risk patient particularly in the context of a difficult airway. The use of adjunctive airway devices such as the endotracheal tube introducer may be more difficult with a DLT [163], though difficult endotracheal intubation with a DLT can be aided by the use of adjunctive devices such as the Glidescope video laryngoscope [164] or the Airway Scope [165]. Additionally, some patients may present with anatomic abnormalities of the airway such as subglottic stenosis or extrinsic compression of the trachea or either mainstem bronchus. Passage of a DLT may be difficult or even dangerous in this context. If it is likely that the patient will require postoperative mechanical ventilation or if extubation is delayed for another reason, exchanging the DLT for a single lumen tube at the end of surgery places the patient at additional risk for loss of airway and aspiration.

The above limitations of DLT have prompted interest in the use of endobronchial blockers for esophageal surgeries. A detailed discussion of endobronchial blockers and their applications can be found in Chaps. 16 and 17. Endobronchial blockers are placed through (coaxially) or occasionally alongside single lumen endotracheal tubes (SLT) and can be used in patients with tracheostomies. The use of endobronchial blockers is well described for thoracic procedures, including esophageal surgery [166] and is preferred by some authors [163]

because of the perceived reduction in aspiration risk with the use of the SLT and rapid sequence induction, the improved ease of managing difficult airways, and lung collapse scores equivalent to that of the DLT [167].

Fluid Management

Fluid requirements vary widely between patients and procedures and ultimately represent the sum of preoperative deficits, maintenance requirements, and ongoing losses. Preoperative fluid deficits in patients with severe esophageal disease may be substantial, though they have not been well defined. Fluid requirements in patients undergoing esophageal procedures may be complicated by the fact that patients may be relatively hypovolemic after long preoperative fasts, particularly if esophageal obstruction or dysphagia limit fluid intake. Perioperative losses occur via a number of mechanisms including urinary, gastrointestinal, and evaporative losses, bleeding, and interstitial fluid shifting. This shift of fluid from the vascular compartment into the interstitial space accompanies surgical trauma and is likely to reflect vascular injury and loss of endothelial integrity. So called “third space” losses describe fluid loss into noninterstitial extracellular spaces which are not in equilibrium with the vascular compartment and thus considered to be a “nonfunctional” extracellular fluid compartment. This space has not been well characterized and its existence has been questioned [168].

In general, minor procedures and those involving minimally invasive surgical procedures tend to be associated with low fluid requirements. Patients undergoing longer and more complex procedures involving open abdominal and/or thoracic incisions may require significantly more intraoperative fluid to maintain homeostasis. Despite many studies in the area of perioperative fluid balance and fluid therapy, a consensus of best practice does not yet exist. However, recent advances in understanding the pathophysiology of fluid shifting in the perioperative setting, advances in the clinical management of fluid balance, and the application of advanced monitoring modalities to drive rational goal directed fluid therapies (GDFTs) justify several conclusions.

First, excessive perioperative intravenous fluid administration, particularly crystalloid, is likely to contribute to an exaggerated fluid shifting towards the interstitial space, potentially increasing complications associated with poor wound healing, slower return of GI function, abdominal compartment syndrome, impaired anastomotic healing, increased cardiac demand, pneumonia, and respiratory failure [169]. Prospective trials examining “liberal” vs. “restrictive” fluid regimens in patients undergoing major surgical procedures generally favor greater fluid restriction [170–172] as do retrospective studies of patients undergoing pulmonary resection surgery [173–175] and esophagectomy [176, 177]. Interpretation of these prospective trials is limited, however, by a lack of standard definition of the terms “restrictive” and “liberal.” What is liberal in one study may be restrictive in another. Retrospective analyses

are limited in this regard by the potential for uncontrolled bias. Most studies of both types, however, are consistent with the idea that crystalloid overload rather than fluid overload, *per se*, is most closely related to adverse outcomes, but these studies do not permit identification of a suitable fluid regimen most compatible with favorable outcomes. However, inadequate fluid resuscitation in patients with significant fluid losses may cause hypovolemia and subsequently, a decrement in stroke volume, cardiac output, and tissue oxygen delivery which could compromise renal function, wound healing, anastomotic integrity, and even cardiovascular stability. Optimizing fluid regimens is likely to be dependent upon adequately measuring fluid requirements or surrogates thereof in individual patients rather than relying upon formulas for “restrictive” or “liberal” regimens. While fluid requirements have not been well characterized in patients undergoing esophageal surgery specifically, recent evaluation of crystalloid requirements to maintain the left ventricular end diastolic volume index (LVEDVI) in patients undergoing colorectal surgery has been made. The rate of crystalloid infusion required to maintain LVEDVI in patients undergoing open and laparoscopic colorectal surgery was 5.9 and 3.4 mL/kg/h, respectively [178]. However, inter-individual variability was high, consistent with the need for an individualized approach. Fluid requirements for thoracic surgical procedures or for esophageal surgeries in particular are not known.

Clearly, an ideal fluid regimen for major surgeries including esophageal surgeries is individualized and optimizes cardiac output and oxygen delivery while avoiding excessive fluid administration. There is an emerging body of evidence that fluid therapies which are designed to achieve individualized and specific flow-related hemodynamic endpoints such as stroke volume, cardiac output, or measures of fluid responsiveness such as stroke volume variation (collectively referred to as GDFT) may provide a superior alternative to fixed regimens or those based on static measures of cardiac filling such as central venous pressure which does not predict fluid responsiveness or correlate with circulating blood volume in hospitalized patients [179] or after TTE [180]. GDFT in the setting of major surgery has been shown to reduce the length of stay [181–188], promote earlier return of bowel function [181], reduce postoperative nausea and vomiting (PONV) [181], morbidity [183–185, 189], and vasopressor use [190]. A review of nine studies utilizing GDFT revealed that of these, seven reported reduced hospital length of stay, three reported reduced PONV and ileus, and four reported a reduction in complications [191].

The use of GDFT for fluid management in thoracic surgery is currently in its infancy and most available studies are small and have investigated primarily patients undergoing cardiac surgery. In addition to the pulmonary artery catheter-derived cardiac output measurements which are not generally used for most general thoracic surgeries and the transesophageal echocardiographic and esophageal Doppler modalities which are inappropriate for esophageal procedures, a number of

minimally invasive modalities compatible with transthoracic esophageal surgery are available. These include primarily devices that use proprietary algorithms to estimate stroke volume index, cardiac index, and/or stroke volume variation [192–195]. The utility of these modalities in directing GDFT in the context of an open hemithorax and OLV has yet to be demonstrated, but other studies demonstrating clinical advantages of GDFT in intra-abdominal surgeries invite a closer examination of the potential benefits.

In addition to the potential importance of the amount and timing of fluid administration, there is also emerging clinical evidence that the choice of fluid type may be important in affecting clinical outcomes. As above, most studies reporting the adverse effects of excessive perioperative fluid administration to patients undergoing thoracic surgery are consistent with the idea that crystalloid overload, rather than fluid overload per se is related to adverse outcomes. These include retrospective studies of factors affecting adverse outcomes after pulmonary resection [173, 174] and esophagectomy [176, 177] as well as number of prospective studies of perioperative fluid therapy [171, 172, 185]. Colloid therapy has been shown to be superior to crystalloid therapy in prospective trials of goal directed fluid management, improving outcomes and postoperative recovery [196]. Goal directed colloid but not crystalloid fluid therapy improved microcirculatory blood flow in a porcine model of anastomotic colon [197] and increased tissue oxygen tension in patients undergoing abdominal surgery [198]. This finding may be of particular relevance to esophageal surgery where anastomotic integrity may be related to blood flow and oxygen delivery to a potentially flow-compromised gastric tube-esophageal anastomosis. The improved efficacy of colloids in improving patient and surrogate outcomes in GDFT trials may be related to a number of possible factors including a greater effect on plasma volume expansion [199] and putative beneficial effects of colloids, on vascular injury, permeability, and the development of edema [200–205]. Taken together, these studies suggest that it may be preferable to use colloids to minimize fluid shifting across a potentially injured vascular barrier. This topic has been recently and extensively re-examined in a review by Chappell et al. [168] in which the authors make a compelling argument for the use of colloids in the replacement of plasma volume losses due to fluid shifting or bleeding.

The ideal choice of colloid solution for plasma volume expansion in major thoracic surgery (including esophageal surgery) also requires further elucidation. However, a number of theoretical advantages of the synthetic colloids have begun to emerge in preclinical studies. These include inhibition of endothelial–leukocyte interactions [206, 207], transendothelial migration of neutrophils [208], and vascular fluid flux [209]. The primary colloid solutions available in the United States for this purpose are human albumin, hetastarch, and the (newly available in the United States) third generation tetrastarch, (Voluven) – a lower molecular weight starch with a number of theoretical advantages, including improved clearance in patients with impaired renal function [210], and reduced

adverse effects on renal integrity [211, 212] and coagulation function [213, 214]. Voluven appears to share favorable characteristics of other synthetic colloids on endothelial cell–leukocyte interaction [207] and has been associated with an inhibition of systemic inflammatory mediators and markers of endothelial cell injury and activation in a clinical study of patients undergoing major abdominal surgery [215].

Intraoperative Complications

Intraoperative management of patients undergoing esophageal surgery may be complicated by a variety of surgical and anesthetic problems. Hypotension is not uncommon during major esophageal surgeries and may result from compression of the heart or major vessels, myocardial ischemia, hypovolemia, or use of an indwelling epidural catheter leading to a thoracic sympathectomy.

Hypoxemia during esophageal surgery occurs not infrequently in patients undergoing OLV and typically is due to right to left shunt flow via the nonventilated lung as well as by volume loss and atelectasis in the dependent lung. Less commonly, hypoxemia during transthoracic esophageal surgery results from trauma to the ventilated lung and resultant tension pneumothorax which can be treated surgically by needle or finger puncture of the contralateral pleura. Pulmonary edema can result from fluid overload, cardiac failure, and immunologic reactions to medications and other immunogens including latex. The diagnosis of fluid overload and/or cardiac failure may be difficult in the context of esophageal surgery as transesophageal echocardiography is usually contraindicated or impractical and data from central venous or pulmonary artery catheters, if present, are of limited value in this regard. Electrocardiographic evidence of myocardial ischemia along with pulmonary edema, particularly if it is not responsive to pharmacologic therapy to improve myocardial oxygen supply/demand inequality, may require aborting the surgical procedure, particularly if detected prior to esophagotomy. Rarely, pulmonary embolization can occur with preferential distribution to the ventilated, perfused lung.

Postoperative Management and Complications

Postoperative management of patients after esophageal surgery is largely dependent on the specific procedure performed and the patient's response to anesthesia and surgery. In general, most patients should be suitable for extubation after elective esophageal surgery, particularly those undergoing esophagoscopy and minimally invasive laparoscopic or thoracoscopic surgical procedures. The extubation of patients undergoing esophagectomy procedures will be discussed later. Provided that patients are stable from a hemodynamic and metabolic standpoint and that neuromuscular and respiratory functions are adequate and a plan for suitable analgesia has been initiated, extubation in the OR is generally appropriate. In most cases, dosing of an indwelling thoracic epidural catheter is well tolerated during

wound closure as the intravenous or inhalational anesthetic is reduced. Following suctioning of the oropharynx and NGT, if present, the patient should be allowed to emerge from general anesthesia and extubated following the return of protective airway reflexes. Placing the patient in a 30° head-up position may improve pulmonary ventilation and decrease aspiration risk. If a gastric drain is indicated for the procedure, it should be secured prior to emergence and extubation.

Hypotension occurs not infrequently after esophageal surgery. Causes include inadequate intraoperative plasma volume expansion, hemorrhage, cardiac dysrhythmias, most commonly atrial tachyarrhythmias, pneumothorax, and sympathectomy from use of TEA. Careful hemodynamic assessment of the postoperative patient should permit the distinction between hypovolemia and other causes. Urine output and chest drain output should be carefully followed and hemoglobin concentration monitored in patients suspected of ongoing bleeding. Routine postoperative chest radiography is indicated in patients undergoing transthoracic or transhiatal procedures and when postoperative cardiovascular or respiratory complications are suspected. Most commonly, epidural related sympathectomy is the cause and can be treated by additional fluid repletion, temporary discontinuation of the infusion, supine re-positioning or leg elevation to augment venous return, or reducing the concentration of local anesthetic in the epidural infusion. Occasionally, hemodynamically fragile patients may require substitution of epidural local anesthetic solution with an opioid such as hydromorphone or morphine, though pain control with this regimen is usually suboptimal.

Atrial tachyarrhythmias occur frequently after thoracic surgical procedures, including esophageal surgeries and may result in significant hemodynamic instability due to a rapid ventricular response and/or myocardial ischemia. This complication has been best studied in patients undergoing esophagectomy surgery and will be discussed later. Myocardial ischemia, congestive heart failure, and pulmonary thromboembolic complications are also possible though appropriate patient selection, preoperative cardiovascular evaluation, and thromboprophylaxis should significantly reduce these risks.

Respiratory insufficiency, seen most commonly in patients with baseline impairment of respiratory function, may be related to weakness from inadequate reversal of neuromuscular blockade. Typically, these patients retain carbon dioxide and may become hypercapnic and obtunded. Often, retractions due to upper airway obstruction can be observed. Other causes of hypoventilation such as bronchospasm, aspiration pneumonitis, pulmonary edema, and pneumothorax, and ARDS should be ruled out with the appropriate diagnostic modalities. Inadequate pain control after thoracotomy or laparotomy can also result in splinting with reduced tidal volumes and hypoventilation. Typically, adequate treatment of incisional pain leads to a dramatic improvement in respiratory function. Chest radiography and arterial blood gas analysis should be performed immediately in any patient with acute respiratory decompensation after thoracic surgery.

Anesthetic Considerations for Specific Esophageal Procedures and Disorders

Esophagoscopy

Esophagoscopy may be performed with either a rigid or flexible endoscope and is used for a number of specific diagnostic and therapeutic purposes. In general, most diagnostic esophagoscopies are performed using flexible endoscopes, often in awake sedated patients and frequently in a gastroenterology suite without the care of an anesthesiologist. Conscious sedation performed by a nurse or other assistant under the direction of an endoscopist, usually a gastroenterologist, is most often accomplished with the use of a benzodiazepine such as diazepam or midazolam with or without the addition of an opioid such as meperidine. Patient acceptance of the procedure without sedation, even with ultrathin esophagoscopes, is quite limited [216]. Often, a local anesthetic such as lidocaine or benzocaine is applied topically to facilitate patient acceptance and reduce gagging during the procedure. If local anesthetic is used, the total acceptable dose should be carefully considered as methemoglobinemia has been associated with topical use of benzocaine for surgical procedures [217], including esophagogastroduodenoscopy (EGD) [218]. Flexible esophagoscopy is also routinely performed by thoracic surgeons immediately prior to esophageal surgery to assess the location and extent of esophageal lesions and the degree of esophageal obstruction. Most of these patients have known esophageal disease and are presenting for curative or palliative esophageal surgery. These patients are usually at elevated risk for regurgitation and aspiration and should be treated appropriately. The airway should be secured prior to instrumentation of the esophagus under general anesthesia.

Rigid esophagoscopy is most frequently employed for the extraction of esophageal foreign bodies, often in children, as well as for the removal of retained food items. As with laryngoscopy, this is a very stimulating procedure and not likely to be well tolerated without general anesthesia. These patients should also be considered high risk for aspiration and managed accordingly, with the rapid placement of a cuffed endotracheal tube before or immediately after induction of anesthesia. In selected patients who are felt to be at lower risk for aspiration with this procedure and who meet NPO guidelines, it may be appropriate to consider deeper levels of sedation. Monitored anesthesia care with sedation using dexmedetomidine infusion for rigid esophagoscopy and dilation of the UES with botulinum toxin injection for dysphagia has been described [219]. Anesthetic management considerations for rigid esophagoscopy include the extreme neck extension desired by surgeons for alignment of the oral–esophageal axis, the risk of aspirating objects once extracted from the esophagus [220], and the need for a relaxed patient to minimize movement during the procedure. The latter need can be achieved with deep levels of inhalational anesthetic or with short-acting muscle relaxants.

Additional therapeutic uses of esophagoscopy include esophageal stent placement for TEF, benign and malignant strictures [221, 222], and perforation [14, 223]. Nonsurgical treatment of achalasia, including esophageal dilatation and intraesophageal delivery of botulinum toxin can also be accomplished endoscopically [224]. Endoscopic techniques are also used in the staging of superficial esophageal tumors and complete resection of mucosal adenocarcinoma [59–62].

Tracheoesophageal Fistula (TEF)

Anesthetic management of the patient with TEF is uniquely challenging for the following reasons. First, positive pressure ventilation inevitably results in ventilatory gas entering the esophagus and stomach. Ventilation of the gastrointestinal tract may result in worsening pulmonary compliance because of abdominal distention and a concomitant increase in the risk of further aspiration and other complications [43, 225, 226]. For these reasons, maintenance of spontaneous ventilation is usually preferred and can be accomplished with either an inhalational induction or an awake intubation, though baseline decrements in pulmonary function and compliance on the affected side are likely to increase difficulties associated with oxygenation and adequate ventilation after induction of anesthesia. The preoperative placement of a gastrostomy tube will aid in venting the stomach in the event that positive pressure ventilation becomes necessary but is contraindicated if the stomach is to be used as a conduit within the thorax. Additionally, chronic aspiration and its sequelae of pneumonia, sepsis, and hypoxemia may complicate the anesthetic management of these patients, particularly during OLV. Positive pressure ventilation can be safely performed once lung isolation has been accomplished. Lung isolation is essential to prevent ventilation of the fistula, to provide adequate pulmonary ventilation, and to prevent further soiling of the lung.

The anesthetic plan for airway management and ventilation in adult patients with TEF should reflect the anatomic position of the fistula in the respiratory tract. Typically, the identification and localization of the fistula is made before presentation to the operating theater. Occasionally, the exact level of the fistula is not known. Though not always successful, bronchoscopic examination of the airway may identify the level of airway involvement and can be performed preoperatively. Bronchoscopy can also be performed after tracheal intubation with either a DLT [227] or SLT [228] and used to guide placement after localization of the TEF.

The DLT is preferred in most cases of TEF since it can be placed into the mainstem bronchus contralateral to the fistula, providing lung isolation, OLV, and protection from soiling of the ventilated lung. Thus, right-sided DLT should be used for left-sided lesions and vice versa. Occasionally, for a tracheal TEF well above the carina, a SLT may be used if the cuff can be inflated below the fistula. If this is not possible, a right DLT is preferable for distal tracheal fistulae or if the fistula site is not identified preoperatively. In patients with severe pulmonary

disease, OLV may be incompatible with adequate oxygenation and ventilation. Rarely, alternative approaches for oxygenation and ventilation that minimize gas flow into the esophagus may be required. The use of a left DLT for lung isolation with high frequency oscillation ventilation on the right side has been described for optimizing gas exchange in a patient with a low tracheal TEF and ARDS [229]. An alternative approach in critically ill ventilated patients with benign TEF utilizes temporary stenting to functionally separate the airway and esophagus, minimizing air leak, and improving CO₂ removal [49]. This procedure was easily performed and well tolerated and could presumably serve as a bridge to definitive surgical correction following improvement in the patient's status.

Postoperative goals include optimizing pulmonary function to facilitate a return to spontaneous ventilation with adequate gas exchange. The continuation of positive pressure ventilation may lead to disruption of the esophageal closure and could thus cause a ventilatory leak. Achieving this goal requires adequate pain control and may also require aggressive pulmonary toilet with bronchoscopy prior to emergence.

Transthoracic Nissen and Belsey Fundoplication, Collis Gastroplasty, and Paraesophageal Hernia Repair

Transthoracic antireflux procedures require monitoring, arterial and venous access commensurate with an open thoracotomy but are otherwise without many specific implications for the anesthesiologist. Lung isolation and OLV is required as is an aggressive plan for postoperative pain control, ideally TEA. Following induction, intubation, and placement of vascular cannulae, the patient is placed in the right lateral decubitus position. It may be desirable to decompress the stomach at this point, particularly if significant amounts of air were introduced during mask ventilation. After withdrawing an indwelling gastric tube, a large bougie/dilator is advanced into the esophagus at the surgeon's request to facilitate the fundoplication. The dilator should be well lubricated with a water soluble lubricant and passed atraumatically into the upper esophagus with manual guidance or with the use of a laryngoscope to aid engagement with the esophageal orifice. Caution should be exercised during advancement and communication with the surgeon is important, particularly if resistance is encountered as esophageal disruption can occur. It is then passed slowly through the esophago-gastric junction and left in this position until the fundoplication sutures are secured at which time it can be withdrawn.

Unless complications are encountered intraoperatively, most patients can be allowed to emerge from anesthesia at the conclusion of surgery and extubated at emergence. The stomach should be drained with a NGT postoperatively. Oral feeding is begun after return of normal bowel activity which may require several days after open repair. Dysphagia to solid foods can be experienced by some patients for several weeks after surgery and is more common with transthoracic procedures and total fundoplications but typically resolves spontaneously.

Esophagectomy

Transhiatal Esophagectomy (THE)

Patients presenting for this procedure require standard monitoring plus a Foley catheter and arterial catheter for continuous arterial blood pressure monitoring. Patients will also benefit from the preoperative placement of an epidural catheter. After preoxygenation and induction of general anesthesia, the trachea is intubated with a SLT and both arterial and adequate intravenous access is obtained – generally two peripheral venous cannulae and an arterial catheter. A NGT is placed and secured in its position after the esophageal anastomosis is made.

The transhiatal approach to esophagectomy requires the manual dissection of the esophagus from the mediastinum blindly via the abdominal hiatus. The manual compression of the heart and great veins commonly causes hypotension, usually transiently. Optimizing volume status prior to this step may partially mitigate the decrement in blood pressure and cardiac output. Close communication between surgeon and anesthesiologist is critical during this stage, as it may become necessary for the surgeon to temporarily discontinue the dissection to permit hemodynamic recovery, particularly in the elderly or fragile patient. The duration of hypotension during dissection may be related to a patient history of cardiac disease and the presence of a midesophageal tumor [230]. The transhiatal dissection may also precipitate atrial and/or ventricular ectopy which could theoretically contribute to hypotension and reduced cardiac output during this phase. Atrial arrhythmias are commonly associated with transhiatal dissection and are more likely in patients with cardiac disease [230]. In a small study of transhiatal esophagectomies, arrhythmias occurred during transhiatal manipulation in 65% of cases, but were transient, did not require treatment, and were not correlated with hypotension [231]. Other potential intraoperative complications include pneumothorax, mediastinal bleeding from injuries to the aorta or azygous vein, and injury of the membranous trachea. Pneumothorax is easily managed surgically with the placement of a tube thoracostomy from the operative field. Massive hemorrhage is rare but is likely to require emergent thoracotomy and repair with aggressive transfusion and resuscitation. Tracheal injury also requires definitive repair and the anesthesiologist may be required to advance the endotracheal tube beyond the site of injury to facilitate ventilation during the repair. For this reason, only full-length uncut endotracheal tubes should be used for THE.

Following completion of the cervical anastomosis and wound closure, the NGT is secured in position. If *in situ*, the epidural catheter should be appropriately dosed prior to emergence. Tracheal extubation is performed at emergence with return of protective airway reflexes and the patient is transferred to a unit where appropriate monitoring and pain control can be accomplished. The head of the bed should be elevated between 30 and 45° to optimize respiratory mechanics and to minimize the potential for reflux and aspiration. Postoperative therapy includes antibiotics and thromboprophylaxis.

Postoperative complications attributable to the THE include recurrent laryngeal nerve injury which results in hoarseness and an increased risk of aspiration pneumonitis, chylothorax, and anastomotic leak.

Transthoracic Esophagectomy (Ivor Lewis; TTE)

Unless contraindicated, a thoracic epidural catheter should be placed preoperatively. Induction and maintenance of general anesthesia can be accomplished with standard agents. For the reasons enumerated earlier, a rapid sequence induction is recommended and endotracheal intubation should ideally be accomplished with attention to the risks of aspiration. Lung isolation is not required for laparotomy and thus, some practitioners intubate initially with a SLT, replacing it with a DLT prior to the thoracotomy incision and after suctioning of the stomach. It is also reasonable to place a DLT at induction unless difficult placement is predicted in a patient with elevated risk of aspiration, such as high-grade obstruction, gastroparesis, or emergency surgery. In such a case, the practitioner should first rapidly secure the airway with a SLT, evacuate stomach contents intraoperatively, and then either place a DLT prior to thoracotomy or simply use an endobronchial blocker.

After induction, an NGT is placed with consideration to possible partial or complete esophageal obstruction that may necessitate surgical assistance for positioning distally. Decompression of the stomach and esophageal conduit is of paramount importance; thus the NGT should be secured intraoperatively to prevent its removal by the patient or inadvertent removal during patient movement and transport. Muscle relaxation with nondepolarizing muscle relaxants provides optimal operating conditions. An arterial catheter and large bore peripheral or central venous access should be obtained after induction.

Intraoperative hypotension occurs not infrequently during TTE surgery and usually results from hypovolemia and/or TEA-related sympathectomy. Hypotension may precipitate myocardial or cerebral ischemia and may also contribute to gastric tube ischemia. Thus, potential causes should be immediately sought and treated. The mobilized gastric tube has a limited blood supply, usually from the right gastroepiploic artery and blood flow at the distal segment is decreased. Factors such as hypotension may further compromise perfusion of the gastric tube and may thus increase the risk of anastomotic leak. Since anastomotic integrity is dependent upon adequate blood flow and oxygen delivery [232–234], the development of anastomotic leak may be related to intraoperative management variables, particularly systemic blood pressure and cardiac output and may thus be modifiable by anesthetic management.

Some esophageal surgeons eschew the use of vasoconstricting agents for fear of the theoretical adverse effects on gastric tube blood flow, though the limited available data do not support this reasoning. The effect of vasoconstrictors on gastric tube blood flow has not been well studied, but a small clinical study by Al-Rawi et al. demonstrated that a TEA-induced

sympathectomy decreased gastric tube blood flow during esophagectomy and that IV infusion of epinephrine restored blood flow [235]. The use of norepinephrine to maintain arterial blood pressure during esophagectomy as part of a multimodal anesthetic regimen has been associated with reduced respiratory morbidity without increasing the incidence of anastomotic complications [111]. Given the established relationship between gastric tube blood flow and anastomotic leak [232, 234, 236], maintenance of normal hemodynamics should be a priority in the intraoperative management of these patients. Towards this end it may be prudent to postpone dosing the indwelling epidural catheter in a hypotensive patient and to consider the use of inotropic agents with or without vasopressor activity.

Following uneventful TTE, most patients can be extubated in the operating room provided that they are normothermic, metabolically and hemodynamically stable, well oxygenated, and pain control modalities have been employed. Although an older randomized trial comparing early vs. late extubation after esophagectomy reported a higher mortality in the early extubation group, this difference was not statistically significant [237] and has not been observed subsequently. Early extubation after esophagectomy has been well studied and is supported by a number of retrospective and observational analyses [108, 238, 239] as well as reports of standardized management approaches [109] and fast track clinical pathways [108, 110, 240]. Factors which may predict failure or complications associated with early extubation include a history of smoking and chronic obstructive pulmonary disease (COPD) [241]. Epidural analgesia may facilitate successful early extubation [108, 239, 241].

At emergence, patients should be seated 30° above supine and extubated upon return of protective airway reflexes. Supplemental oxygen may be delivered via face tent or nasal cannulae. If postoperative ventilatory support is required or extubation must be delayed for other reasons, tube exchange can be performed with laryngoscopy, adjunctive airway devices, or via a tube exchange catheter.

Minimally Invasive Esophagectomy (MIE)

At this time, there is little specific data available to guide anesthetic management of the patient undergoing MIE but principles of management in the patient undergoing open esophagectomy are likely to apply. OLV is considered essential for any thoracoscopic procedure, including MIE and thus, lung isolation is required. The use of DLT and bronchial blockers for esophageal surgery has been discussed earlier and applies here as well. Because of the longer duration of MIE surgery, a DLT is preferred as bronchial blockers are less stable positionally [167] and are likely to require more frequent repositioning.

Avoiding a large thoracotomy incision in the context of MIE might conceivably reduce major pulmonary complications after esophagectomy. Though high quality comparative studies are few and randomized controlled trials are completely

lacking, a systematic review of the available studies indicates an overall incidence of pulmonary complications of 22.9% in TTE and 15.1% in MIE [242]. Rigorous comparison to the TTE awaits adequately powered prospective trials. It is not clear that patients undergoing MIE require aggressive pain control modalities such as TEA for optimal postoperative pain control. However, the TEA remains the standard of care in centers which perform these surgeries largely because of the theoretical and demonstrated advantages of TEA in the context of open esophagectomy and thoracic surgery in general.

Postoperative Care of the Esophagectomy Patient

With appropriate pain control regimens, most patients are extubated in the operating room. Early ambulation and chest physiotherapy are used to reduce respiratory complications. Pleural drains are removed as soon as drainage is minimal and absence of air leak is confirmed, though mediastinal drains may be left until confirmation of intrathoracic anastomotic integrity is confirmed. The indwelling epidural catheter is generally used and left in situ until pleural drains are removed, at which time pain control can be adequately accomplished with parenteral or enteral medications. Feeding via jejunostomy tubes is initiated after 24 h postoperatively and advanced over a period of several days. A contrast study of the esophagus is usually performed on or about the fifth postoperative day and if normal, a clear diet by mouth is begun at that time. At discharge, the patient will be eating solid food and the jejunostomy tube is clamped. At surgical follow-up in several weeks, the feeding tube is removed.

Adverse Outcomes After Esophagectomy

Adverse outcomes after esophagectomy surgery have historically been divided into surgical and anesthetic complications. At first glance, this division is logical and appealing, but recent insight into the pathophysiology of complications after major thoracic and thoracoabdominal surgeries is beginning to blur this distinction.

Esophageal Anastomotic Leaks

As mentioned earlier, the development of an esophageal anastomotic leak is a frequent and serious complication of esophagectomy. This complication is particularly worrisome when the leak is mediastinal in location. Mortality rates from intrathoracic leaks range from 3.3 to 71% [243]. Preoperative, operative, and postoperative factors that may predispose to the development of anastomotic leak have been well described in the literature [243] and include comorbidities such as diabetes, pulmonary disease, and cardiovascular disease; a variety of surgical and technical factors; and postoperative factors including gastric distension, prolonged ventilatory support, and hypoxia. Though still considered a surgical complication, accumulating evidence suggests that intraoperative management may have an impact on the incidence of this complication. Because of

the tenuous blood supply to the mobilized gastric tube, fluid status, hemodynamics, and oxygenation may affect anastomotic integrity through effects on oxygen delivery [232, 233] and blood flow [232]. Though the optimization of tissue oxygen delivery through appropriate management of hemodynamics, fluid status, and oxygenation is a priority for all perioperative patients, this truism may be particularly critical for patients undergoing esophageal anastomoses.

Cardiovascular Complications

Cardiovascular complications account for significant morbidity and mortality after esophagectomy. The most common cardiac complication is arrhythmia, typically atrial tachyarrhythmias such as atrial fibrillation, atrial flutter, and paroxysmal supraventricular tachycardia. While generally considered benign after cardiac surgery, these diagnoses may be more ominous after general thoracic surgery including esophagectomy. There is considerable evidence that atrial tachyarrhythmias after esophagectomy are associated with a higher rate of ICU admission, greater length of hospital stay, and a higher mortality [244, 245]. These findings are consistent with those for general noncardiac thoracic surgery patients in whom atrial fibrillation was a marker for increased morbidity and mortality [246]. Atrial fibrillation after esophagectomy is also associated with a higher rate of pulmonary complications, anastomotic leakage, and sepsis [245]. Risk factors for the development of atrial dysrhythmias after esophagectomy include older age, perioperative theophylline use, a low diffusion capacity [244, 247], COPD, male sex, and history of cardiac disease [247]. Larger studies of general thoracic surgery patients including esophagectomies point to similar risks for the development of atrial fibrillation – male sex, older age, history of congestive heart failure, arrhythmia, peripheral vascular disease and resection of mediastinal tumor, pulmonary resection, esophagectomy, and intraoperative blood transfusion [246].

The prophylaxis of atrial tachyarrhythmias in general thoracic surgery has been the subject of numerous clinical trials and observational studies but no clinical standard for prophylaxis exists. A review of trials of pharmacologic prophylaxis for postoperative atrial arrhythmias reported that calcium channel blockers and beta blockers reduced the risk of tachyarrhythmias, though the latter increased the risk of pulmonary edema [248]. The routine prophylactic use of digoxin, flecainide, and amiodarone is not supported by the available evidence [248]. The available evidence supports individualized prophylaxis in patients at higher risk of atrial tachyarrhythmias after esophagectomy with either calcium channel blockers or beta blockers, with attention to the potential for adverse effects of the latter.

Pulmonary Complications

Respiratory morbidity occurs frequently after thoracic surgery in general and after esophagectomy in particular [107, 249]. Pulmonary complications of thoracic surgery are variably

defined in the literature, but include pneumonia, aspiration pneumonitis, acute lung injury (ALI), ARDS, bronchopleural fistula, atelectasis, and pulmonary embolism. Any individual or cluster of these complications can result in respiratory insufficiency or respiratory failure, which may require specific therapies including the continuation or reinstitution of mechanical ventilation. The overall incidence of serious respiratory morbidity is highly variable but is between 10 and 30% in most large series [250–253]. Factors predictive of pulmonary complications after esophagectomy include age [250, 251], proximal location of esophageal tumor, and duration of surgery [250], as well as forced expiratory volume in 1 s (FEV₁) [251] which predicts pulmonary complications in patients with COPD [254].

ALI and ARDS are among the most severe pulmonary complications associated with esophagectomy and their incidence in a large series was 23.8 and 14.5%, respectively [255]. ARDS was associated with a 50% mortality rate in this series. Risk factors included low body mass index, tobacco history, surgeon experience, duration of surgery and OLV, anastomotic leak, and cardiorespiratory instability. The pathophysiology of ALI and ARDS are complex and thought to result from direct or indirect pulmonary injury. Though injury can occur from a variety of mechanisms, the final pathway appears to involve inflammatory mediators including cytokines and cellular mediators. Still a very active area of investigation, it has become clear that surgical stress itself elicits an already well characterized and profound inflammatory response that includes cytokines such as IL-1, IL-8, TNF-alpha, IL-6, selectins, neutrophil elastase, and thrombomodulin [256–260]. In particular, IL-8 has been implicated in the development of ARDS [261] and is likely to provide a strong signal for the chemotactic migration of neutrophils [262, 263], the alveolar infiltration of which is characteristic of the disease process. The degranulation of neutrophils and an increase in pulmonary capillary permeability has been demonstrated after esophagectomy and has been proposed as a human model of lung injury [260]. Causative involvement of IL-8 is suggested by studies of IL-8 antagonists in animal models [262], the presence of high concentrations in both ventilated and nonventilated lungs [264], and the relationship between IL-8 concentrations in lavage fluid and the subsequent development of pulmonary complications after esophagectomy [265].

Improving Outcomes After Esophagectomy

The use of TEA for postoperative analgesia has been reviewed earlier, but its potential value in improving outcomes after esophagectomy merits additional mention. Improved outcomes associated with the use of TEA after transthoracic esophageal surgery [103–107] may be related to improved postoperative pulmonary function and resultant decrease in pulmonary complications [104] and an improvement in gastric tube blood flow [266, 267]. The use of TEA has been associated with a decreased risk of anastomotic leak in a retrospective study of esophagectomy patients [106]. A causative role is implied by

animal experiments in which the use of TEA improved microcirculation and motility in the gastric tube [267] and a clinical study with similar findings [266]. For these reasons and the overwhelming evidence of superior pain control, TEA represents the standard of care for TTE in most institutions.

Though lung injury in this context is multifactorial, there is a growing awareness that anesthetic and perioperative factors are involved. These include, atelectasis which is obligate in the operative hemithorax during OLV, direct injurious effect of volutrauma or barotrauma in the contralateral lung during OLV, oxygen stress and toxicity resulting from high FIO_2 in the ventilated lung, and ischemia reperfusion injury in the ipsilateral lung after re-ventilation. Strategies to protect the lung and optimize outcomes after major thoracic surgery are most likely to be successful if they minimize these injurious stimuli. Guidance in the absence of definitive outcome data in the perioperative thoracic surgery setting is based largely on results from studies of animal models, surrogate markers of lung injury, and patients with established lung injury. Nonetheless, several reasonable conclusions can be drawn at this time.

First, ventilation strategies, particularly during OLV, should be tailored to patient physiology. That OLV itself may be a factor in the inflammatory response accompanying thoracic esophageal surgery is suggested by studies of cytokine and complement levels during and after OLV [256, 268]. Thus, ventilation should be as physiologic as possible in an effort to minimize the likelihood of volutrauma. So-called protective ventilation strategies represent a physiologic approach to tidal ventilation and are likely to improve outcomes in this patient population by minimizing the risk of alveolar overdistension as well as cyclic collapse of alveoli. Specifically, protective ventilation in the context of thoracic surgery and OLV has referred to lower tidal volumes (4–6 mL/kg ideal body weight) with added positive end expiratory pressure (PEEP). This ventilatory strategy in patients undergoing TTE has been shown to minimize surrogate markers of systemic inflammation (IL-1Beta, IL-6, IL-8) [256, 269] while improving oxygenation intra- and postoperatively, and decreasing the duration of mechanical ventilation [256]. Specific protective pharmacologic agents have not been well studied, though there is preliminary data suggesting that prostaglandin E1 may also lead to a reduction in the inflammatory response [270] and improvements in gastric tube [271] and tracheal [272] blood flow in esophagectomy. Since oxygen toxicity and oxidative stress may also contribute to the development of adverse outcomes, it may be prudent to minimize FIO_2 , though the large obligate right to left shunt in the nonventilated lung during OLV limits the extent to which this maneuver is practicable.

It is clear that anesthetics themselves may modify the inflammatory response to surgical stimulation and trauma [273] and produce other specific and in some cases, desirable biologic effects such as myocardial protection. Recent evidence suggests that sevoflurane may also affect lung tissue by modulating the inflammatory response to OLV. De Conno et al. demonstrated

an attenuated increase in the bronchoalveolar lavage levels of TNF-alpha, IL-6, IL-8, MCP-1 in patients anesthetized with sevoflurane vs. propofol [274]. This immunomodulation was accompanied by a reduction in adverse clinical events suggesting a protective role of sevoflurane.

Surgery for Esophageal Rupture and Perforation

Patients presenting for emergent repair of esophageal disruption, rupture, or perforation may present with pain, hypovolemia, sepsis, and shock. Anesthetic management should be based on the severity of these presenting conditions and the nature of the planned procedure. To the extent possible, fluid deficits should be corrected preoperatively and may be guided by standard and invasive monitoring as appropriate. Because of the likelihood of further fluid losses and hemodynamic decompensation, an arterial catheter for continuous blood pressure monitoring and arterial blood gas sampling is indicated.

The principles of anesthetic management are based on correcting preoperative fluid deficits, minimizing hemodynamic derangements, avoiding increases in abdominal pressure which may exacerbate leakage of gastroesophageal contents, and minimizing the risk of aspiration, particularly during induction. In general, a rapid sequence induction is indicated with the choice and dose of induction and neuromuscular blocking agents tailored to the patient's hemodynamic status. If a thoracotomy is planned or likely, surgical exposure will benefit from the use of a DLT, but this advantage should be considered in light of airway anatomy, anticipated ease of intubation, and the potentially elevated risk of aspiration should placement of the DLT require additional time.

Intraoperative management is likely to be dominated by the need for continuous fluid resuscitation. Arterial blood gas analysis and pulmonary artery catheter data may be used to guide fluid management and plasma volume expansion as well as the likely need for blood products. This factor combined with the probability of ongoing fluid shifts, pulmonary edema, and the need for inotropic and vasopressor support usually mandates postoperative ventilatory support.

Surgery for Achalasia

Esophagomyotomy is most commonly performed to relieve esophageal obstruction at the sphincter level as well as for the relief of pain from esophageal spasm. Esophagomyotomy can be performed laparoscopically, thoracoscopically, or via thoracotomy, with or without the addition of an antireflux procedure. Either transthoracic procedure requires a suitable plan for lung isolation and postoperative pain control, though a TEA may not be absolutely essential for the thoracoscopic esophagomyotomy. Arguably, the most important anesthetic consideration is the possibility of aspiration on induction of anesthesia with loss of protective airway reflexes. Because achalasia results in a dilated esophagus with impaired motility, the likelihood

of retained food material in the esophagus is dramatically increased. It may also be desirable to restrict oral intake to only clear liquids for 2 days prior to surgery in an effort to reduce food retention. Approaches to minimize the risk of regurgitation and aspiration have been discussed previously and are especially important in these patients.

Additional anesthetic considerations for esophagomyotomy procedures include pain control and lung isolation. The use of thoracoscopy to perform a transthoracic myotomy undoubtedly reduces pain intensity and may not require TEA, though many practitioners still prefer it. After induction and intubation with a DLT or SLT with blocker and placement of a NGT, the patient is turned in the lateral decubitus position, usually right lateral decubitus and the transthoracic myotomy is performed. Most patients can be extubated in the operating room after return of protective airway reflexes. The NGT is usually removed and feedings initiated and advanced after the return of normal peristaltic activity.

Surgery for Esophageal Diverticula

Zenker's Diverticulum

While Zenker's diverticulum is not a disorder of the thoracic esophagus, its repair is often undertaken by thoracic surgeons and so it will be briefly discussed. Anesthetic management of patients with Zenker's diverticulum should be focused on the prevention of aspiration. Patients should be restricted to clear liquids for at least 24 h preoperatively and encouraged to manually express and empty the diverticulum prior to anesthetic induction if this is possible. Other efforts to avoid aspiration of diverticular contents include a head-up position (30°) during induction and a rapid sequence induction without cricoid pressure. In the patient with difficult airway anatomy it may be preferable to intubate the trachea prior to induction of anesthesia. Caution should be exercised during placement of a gastric drain tube or esophageal bougie as these may enter the diverticulum and cause perforation.

Thoracic Diverticula

Patients presenting with thoracic esophageal diverticula may represent a subclass of patients at the highest risk for aspiration in the perioperative period. The reasons for this are twofold. First, these diverticula may be large and potentially contain significant quantities of food material. Secondly, these diverticula cannot be emptied by manual expression, though drainage may be possible with the careful placement of a large bore drain tube. Additionally, most thoracic diverticula are associated with an esophageal motility disorder such as achalasia which is itself, a high-risk condition with regard to aspiration. Thus, all reasonable precautions should be taken, including a head-up position, and either a rapid sequence induction or an awake intubation depending on the anticipated ease of airway management.

Transthoracic repair of esophageal diverticula is usually accomplished via a left thoracotomy incision. Surgical exposure is facilitated by lung isolation and OLV. During dissection, the anesthesiologist may assist by passing a large esophageal bougie with surgical guidance until it passes the diverticular aperture. If not already in situ, a NG tube should be placed prior to emergence and should remain in place until esophageal integrity has been demonstrated by a contrast esophagram several days postoperatively. Most patients presenting for elective transthoracic resection of esophageal diverticula can be extubated following the procedure provided that a suitable plan for pain control has been initiated.

Clinical Case Discussion (Fig. 30.7)

Case: A 61-year-old male presents with a 14-month history of episodic dysphagia to solids that is progressively worsening. He notes no pain or weight loss. His evaluation included an EGD and biopsy showing high-grade dysplasia with features highly suspicious for invasive esophageal adenocarcinoma. Further evaluation in preparation for surgery included a whole-body PET-CT scan following injection of 14.014 mCi of F-18-FDG intravenously. Figure 30.7 shows the distal esophageal lesion illuminated by the marker. His past medical history is significant for CAD (MI 12 years prior treated with angioplasty). He has not had a recent cardiac catheterization. He also has intermittent supraventricular tachycardia (PSVT) controlled with diltiazem. He denies ever having an electrophysiologic study performed. He also suffers from HTN (enalapril), hypercholesterolemia (simvastatin), and asthma (albuterol as needed and Claritin). His only surgery has been a C4–7 discectomy and fusion and a L4–S1 laminectomy. He is scheduled for an Ivor-Lewis esophagectomy.

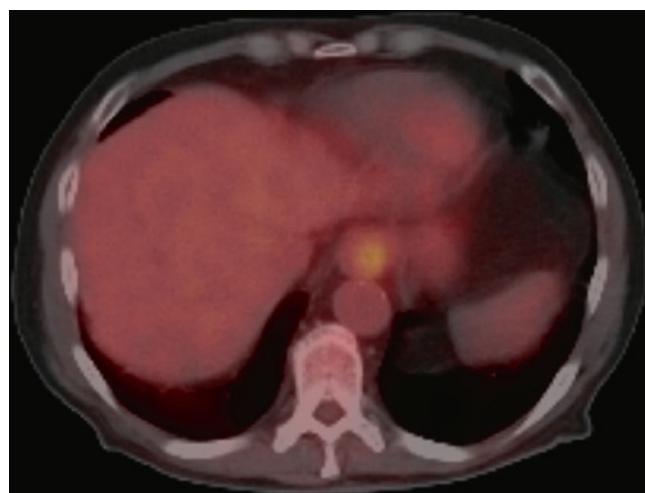


FIG. 30.7. PET scan reveals focal soft tissue thickening with increased uptake of FDG in the distal esophagus at the gastroesophageal junction consistent with esophageal carcinoma.

Questions

- What further preoperative evaluation might be considered reasonable?
- What are the anesthetic considerations for this esophageal surgery?
- What specific intraoperative management strategies might be prudent in this patient?

Focused Preoperative History, Physical, and Investigations

- Patient reports a daily requirement for his MDI and has recovered recently from a viral pharyngitis (physical exam, preoperative MDI use) (see Chap. 8).
- Cardiac evaluation: baseline ECG to evaluate impulse initiation site, AV node conduction, and QTc in the context of PSVT history and diltiazem use. Stress echocardiogram to evaluate audible murmur and ventricular function (see Chap. 2).
- Careful airway evaluation with particular attention to cervical extension after cervical fusion.
- Focused neurologic exam to identify any preoperative deficits given the risk of position-related neurologic injury in left lateral decubitus position (see Chaps. 17 and 18).

What Intraoperative Management Considerations Will Optimize the Patient's Surgery?

- Thoracic epidural to provide postoperative analgesia for a right thoracotomy and upper midline laparotomy (see Chaps. 30 and 46).
- Avoidance of beta-blockade because of a significant history of reactive airway disease and chronic calcium channel blockade use. Intraoperative application of external electrodes for emergency cardioversion, pacing, or defibrillation. Calcium channel blockers indicated for treating hemodynamically stable PSVT (see Chap. 8).
- Fluid management strategy which seeks to optimize overall oxygen delivery, with particular attention to the high-risk esophageal anastomosis. A variety of methods can be used to guide fluid therapy (base deficit, serum lactate, mixed venous O₂ saturation). Optimal fluid management will seek to optimize cardiac output and oxygen delivery while avoiding excessive fluid administration.
- High postoperative risk of atrial arrhythmias, in particular, atrial fibrillation. Treatment usually includes rate control with a beta blocker especially in the patient with CAD but preoperative use of a calcium channel blocker and history of asthma may preclude its use. Amiodarone can be used if atrial fibrillation is sustained and resistant to rate control with calcium channel blockers (see Chap. 41).

References

1. Fein M, Ritter MP, DeMeester TR, et al. Role of the lower esophageal sphincter and hiatal hernia in the pathogenesis of gastroesophageal reflux disease. *J Gastrointest Surg.* 1999;3(4):405–10.
2. Skinner DB. Hernias (hiatal, traumatic, and congenital). 4th ed. Philadelphia: W.B. Saunders; 1985.
3. Halpin VJ, Soper NJ. Paraesophageal hernia. *Curr Treat Options Gastroenterol.* 2001;4(1):83–8.
4. Dassinger MS, Torquati A, Houston HL, Holzman MD, Sharp KW, Richards WO. Laparoscopic fundoplication: 5-year follow-up. *Am Surg.* 2004;70(8):691–4. discussion 694–5.
5. Cowgill SM, Arnaoutakis D, Villalpando D, et al. Results after laparoscopic fundoplication: does age matter? *Am Surg.* 2006;72(9):778–83. discussion 774–83.
6. Ritter MP, Peters JH, DeMeester TR, et al. Treatment of advanced gastroesophageal reflux disease with Collis gastroplasty and Belsey partial fundoplication. *Arch Surg.* 1998;133(5):523–8. discussion 528–9.
7. Patel HJ, Tan BB, Yee J, Orringer MB, Iannettoni MD. A 25-year experience with open primary transthoracic repair of paraesophageal hiatal hernia. *J Thorac Cardiovasc Surg.* 2004;127(3):843–9.
8. Gangopadhyay N, Perrone JM, Soper NJ, et al. Outcomes of laparoscopic paraesophageal hernia repair in elderly and high-risk patients. *Surgery.* 2006;140(4):491–8. discussion 498–9.
9. Khan AZ, Strauss D, Mason RC. Boerhaave's syndrome: diagnosis and surgical management. *Surgeon.* 2007;5(1):39–44.
10. Nesbitt JC, Sawyers JL. Surgical management of esophageal perforation. *Am Surg.* 1987;53(4):183–91.
11. Han SY, McElvein RB, Aldrete JS, Tishler JM. Perforation of the esophagus: correlation of site and cause with plain film findings. *AJR Am J Roentgenol.* 1985;145(3):537–40.
12. Abbas G, Schuchert MJ, Pettiford BL, et al. Contemporaneous management of esophageal perforation. *Surgery.* 2009;146(4):749–55. discussion 746–55.
13. Vogel SB, Rout WR, Martin TD, Abbott PL. Esophageal perforation in adults: aggressive, conservative treatment lowers morbidity and mortality. *Ann Surg.* 2005;241(6):1016–21. discussion 1013–21.
14. Fischer A, Thomusch O, Benz S, von Dobschuetz E, Baier P, Hopt UT. Nonoperative treatment of 15 benign esophageal perforations with self-expandable covered metal stents. *Ann Thorac Surg.* 2006;81(2):467–72.
15. Gelbmann CM, Ratiu NL, Rath HC, et al. Use of self-expandable plastic stents for the treatment of esophageal perforations and symptomatic anastomotic leaks. *Endoscopy.* 2004;36(8):695–9.
16. Siersema PD, Homs MY, Haringsma J, Tilanus HW, Kuipers EJ. Use of large-diameter metallic stents to seal traumatic nonmalignant perforations of the esophagus. *Gastrointest Endosc.* 2003;58(3):356–61.
17. Podas T, Eaden J, Mayberry M, Mayberry J. Achalasia: a critical review of epidemiological studies. *Am J Gastroenterol.* 1998;93(12):2345–7.
18. Kraichely RE, Farrugia G. Achalasia: physiology and etiopathogenesis. *Dis Esophagus.* 2006;19(4):213–23.
19. de Oliveira RB, Rezende Filho J, Dantas RO, Iazigi N. The spectrum of esophageal motor disorders in Chagas' disease. *Am J Gastroenterol.* 1995;90(7):1119–24.

20. Williams VA, Peters JH. Achalasia of the esophagus: a surgical disease. *J Am Coll Surg.* 2009;208(1):151–62.
21. Ott DJ, Richter JE, Chen YM, Wu WC, Gelfand DW, Castell DO. Esophageal radiography and manometry: correlation in 172 patients with dysphagia. *AJR Am J Roentgenol.* 1987;149(2):307–11.
22. Campos GM, Vittinghoff E, Rabl C, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. *Ann Surg.* 2009;249(1):45–57.
23. Finley RJ. Achalasia: thoracoscopic and laparoscopic myotomy. 2nd ed. Philadelphia: Churchill Livingstone; 2002.
24. Heitmiller RF, Buzdon MM. Surgery for achalasia and other motility disorders. 2nd ed. Philadelphia: Lippincott, Williams, and Wilkins; 2007.
25. Stewart KC, Finley RJ, Clifton JC, Graham AJ, Storseth C, Inculet R. Thoracoscopic versus laparoscopic modified Heller Myotomy for achalasia: efficacy and safety in 87 patients. *J Am Coll Surg.* 1999;189(2):164–9. discussion 169–70.
26. Maher JW. Thoracoscopic esophagomyotomy for achalasia: maximum gain, minimal pain. *Surgery.* 1997;122(4):836–40. discussion 831–40.
27. Maher JW, Conklin J, Heitshusen DS. Thoracoscopic esophagomyotomy for achalasia: preoperative patterns of acid reflux and long-term follow-up. *Surgery.* 2001;130(4):570–6. discussion 576–7.
28. Champion JK, Delisle N, Hunt T. Comparison of thoracoscopic and laparoscopic esophagomyotomy with fundoplication for primary motility disorders. *Eur J Cardiothorac Surg.* 1999;16 Suppl 1:S34–6.
29. Rosemurgy A, Villalolid D, Thometz D, et al. Laparoscopic Heller myotomy provides durable relief from achalasia and salvages failures after botox or dilation. *Ann Surg.* 2005;241(5):725–33. discussion 725–33.
30. Costantini M, Zaninotto G, Guirroli E, et al. The laparoscopic Heller-Dor operation remains an effective treatment for esophageal achalasia at a minimum 6-year follow-up. *Surg Endosc.* 2005;19(3):345–51.
31. Gholoum S, Feldman LS, Andrew CG, et al. Relationship between subjective and objective outcome measures after Heller myotomy and Dor fundoplication for achalasia. *Surg Endosc.* 2006;20(2):214–9.
32. Patti MG, Arcerito M, De Pinto M, et al. Comparison of thoracoscopic and laparoscopic Heller myotomy for achalasia. *J Gastrointest Surg.* 1998;2(6):561–6.
33. Patti MG, Pellegrini CA, Horgan S, et al. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. *Ann Surg.* 1999;230(4):587–93. discussion 584–93.
34. Schuchert MJ, Luketich JD, Landreneau RJ, et al. Minimally-invasive esophagomyotomy in 200 consecutive patients: factors influencing postoperative outcomes. *Ann Thorac Surg.* 2008;85(5):1729–34.
35. Mehra M, Bahar RJ, Ament ME, et al. Laparoscopic and thoracoscopic esophagomyotomy for children with achalasia. *J Pediatr Gastroenterol Nutr.* 2001;33(4):466–71.
36. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. *Ann Surg.* 2008;248(6):1023–30.
37. Jeansson LO, White BC, Pilger KE, et al. Ten-year follow-up of laparoscopic Heller myotomy for achalasia shows durability. *Surg Endosc.* 2007;21(9):1498–502.
38. Reed WJ, Doyle SE, Aprahamian C. Tracheoesophageal fistula after blunt chest trauma. *Ann Thorac Surg.* 1995;59(5):1251–6.
39. Drage SM, Pac Soo C, Dexter T. Delayed presentation of tracheo-oesophageal fistula following percutaneous dilatational tracheostomy. *Anaesthesia.* 2002;57(9):932–3.
40. Chang CY, Chang YT, Lee PL, Lin JT. Tracheoesophageal fistula. *Gastrointest Endosc.* 2004;59(7):870.
41. Collier KP, Zubairi RS, Lewis JH. Tracheoesophageal fistula from an indwelling endotracheal tube balloon: a report of two cases and review. *Gastrointest Endosc.* 2000;51(2):231–4.
42. Moaty RC, Rath P, Self M, Dunn E, Mangram A. Review of tracheo-esophageal fistula associated with endotracheal intubation. *J Surg Educ.* 2007;64(4):237–40.
43. Grant DM, Thompson GE. Diagnosis of congenital tracheoesophageal fistula in the adolescent and adult. *Anesthesiology.* 1978;49(2):139–40.
44. Lancaster JL, Hanafi Z, Jackson SR. Adult presentation of a tracheoesophageal fistula with co-existing laryngeal cleft. *J Laryngol Otol.* 1999;113(5):469–72.
45. Zacharias J, Genc O, Goldstraw P. Congenital tracheoesophageal fistulas presenting in adults: presentation of two cases and a synopsis of the literature. *J Thorac Cardiovasc Surg.* 2004;128(2):316–8.
46. Finkelstein RG. The intraoperative diagnosis of a tracheoesophageal fistula in an adult. *Anesthesiology.* 1999;91(6):1946–7.
47. Smith HM, Bacon DR, Sprung J. Difficulty assessing endotracheal tube placement in a patient with undiagnosed iatrogenic tracheoesophageal fistula. *J Cardiothorac Vasc Anesth.* 2006; 20(2):223–4.
48. Balazs A, Kupcsulik PK, Galambos Z. Esophagorespiratory fistulas of tumorous origin. Non-operative management of 264 cases in a 20-year period. *Eur J Cardiothorac Surg.* 2008;34(5):1103–7.
49. Eleftheriadis E, Kotzampassi K. Temporary stenting of acquired benign tracheoesophageal fistulas in critically ill ventilated patients. *Surg Endosc.* 2005;19(6):811–5.
50. Macchiarini P, Verhoye JP, Chapelier A, Fadel E, Darteville P. Evaluation and outcome of different surgical techniques for postintubation tracheoesophageal fistulas. *J Thorac Cardiovasc Surg.* 2000;119(2):268–76.
51. Cassivi SD, Deschamps C, Nichols FC III, Allen MS, Pairolo PC. Diverticula of the esophagus. *Surg Clin North Am.* 2005;85(3):495–503, ix.
52. Rascoe PA, Smythe WR. Excision of esophageal diverticula. 2nd ed. Philadelphia: Lippincott, Williams, and Wilkins; 2007.
53. van Overbeek JJ. Pathogenesis and methods of treatment of Zenker's diverticulum. *Ann Otol Rhinol Laryngol.* 2003;112(7): 583–93.
54. Costantini M, Zaninotto G, Rizzetto C, Narne S, Ancona E. Oesophageal diverticula. *Best Pract Res Clin Gastroenterol.* 2004;18(1):3–17.
55. Visosky AM, Parke RB, Donovan DT. Endoscopic management of Zenker's diverticulum: factors predictive of success or failure. *Ann Otol Rhinol Laryngol.* 2008;117(7):531–7.
56. Varghese Jr TK, Marshall B, Chang AC, Pickens A, Lau CL, Orringer MB. Surgical treatment of epiphrenic diverticula: a 30-year experience. *Ann Thorac Surg.* 2007;84(6):1801–9. discussion 1801–9.
57. Kamangar F, Chow WH, Abnet CC, Dawsey SM. Environmental causes of esophageal cancer. *Gastroenterol Clin North Am.* 2009;38(1):27–57, vii.

58. Liu W, Zhang X, Sun W. Developments in treatment of esophageal/gastric cancer. *Curr Treat Options Oncol.* 2008;9(4–6):375–87.
59. Maish MS, DeMeester SR. Endoscopic mucosal resection as a staging technique to determine the depth of invasion of esophageal adenocarcinoma. *Ann Thorac Surg.* 2004;78(5):1777–82.
60. Prasad GA, Buttar NS, Wongkeesong LM, et al. Significance of neoplastic involvement of margins obtained by endoscopic mucosal resection in Barrett's esophagus. *Am J Gastroenterol.* 2007;102(11):2380–6.
61. Ell C, May A, Pech O, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). *Gastrointest Endosc.* 2007;65(1):3–10.
62. Pech O, Behrens A, May A, et al. Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. *Gut.* 2008;57(9):1200–6.
63. Ilson DH. Esophageal cancer chemotherapy: recent advances. *Gastrointest Cancer Res.* 2008;2(2):85–92.
64. Bleiberg H, Conroy T, Paillot B, et al. Randomised phase II study of cisplatin and 5-fluorouracil (5-FU) versus cisplatin alone in advanced squamous cell oesophageal cancer. *Eur J Cancer.* 1997;33(8):1216–20.
65. Wijnhoven BP, van Lanschot JJ, Tilanus HW, Steyerberg EW, van der Gaast A. Neoadjuvant chemoradiotherapy for esophageal cancer: a review of meta-analyses. *World J Surg.* 2009;33(12):2606–14.
66. Veuillez V, Rougier P, Seitz JF. The multidisciplinary management of gastrointestinal cancer. Multimodal treatment of oesophageal cancer. *Best Pract Res Clin Gastroenterol.* 2007;21(6):947–63.
67. Fernando HC, Murthy SC, Hofstetter W, et al. The Society of Thoracic Surgeons practice guideline series: guidelines for the management of Barrett's esophagus with high-grade dysplasia. *Ann Thorac Surg.* 2009;87(6):1993–2002.
68. Orringer MB, Marshall B, Stirling MC. Transhiatal esophagectomy for benign and malignant disease. *J Thorac Cardiovasc Surg.* 1993;105(2):265–76. discussion 267–76.
69. Ferraro P, Duranteau A. Esophagectomy for benign disease. In: Pearson FG, Cooper JD, Deslauriers J, et al., editors. *Esophageal surgery.* 2nd ed. New York: Churchill Livingstone; 2002. p. 453–64.
70. Orringer MB, Marshall B, Chang AC, Lee J, Pickens A, Lau CL. Two thousand transhiatal esophagectomies: changing trends, lessons learned. *Ann Surg.* 2007;246(3):363–72. discussion 364–72.
71. Hulscher JB, Tijssen JG, Obertop H, van Lanschot JJ. Transthoracic versus transhiatal resection for carcinoma of the esophagus: a meta-analysis. *Ann Thorac Surg.* 2001;72(1):306–13.
72. Hulscher JB, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med.* 2002;347(21):1662–9.
73. Rentz J, Bull D, Harpole D, et al. Transthoracic versus transhiatal esophagectomy: a prospective study of 945 patients. *J Thorac Cardiovasc Surg.* 2003;125(5):114–20.
74. Luketich JD, Alvelo-Rivera M, Buenaventura PO, et al. Minimally invasive esophagectomy: outcomes in 222 patients. *Ann Surg.* 2003;238(4):486–94. discussion 485–94.
75. Urschel JD. Late dysphagia after presternal colon interposition. *Dysphagia.* 1996;11(1):75–7.
76. Cense HA, Visser MR, Van Sandick JW, et al. Quality of life after colon interposition by necessity for esophageal cancer replacement. *J Surg Oncol.* 2004;88(1):32–8.
77. Domreis JS, Jobe BA, Aye RW, Deveney KE, Sheppard BC, Deveney CW. Management of long-term failure after colon interposition for benign disease. *Am J Surg.* 2002;183(5):544–6.
78. Jeyasingham K, Lerut T, Belsey RH. Revisional surgery after colon interposition for benign oesophageal disease. *Dis Esophagus.* 1999;12(1):7–9.
79. de Delva PE, Morse CR, Austen Jr WG, et al. Surgical management of failed colon interposition. *Eur J Cardiothorac Surg.* 2008;34(2):432–7. discussion 437.
80. Doki Y, Okada K, Miyata H, et al. Long-term and short-term evaluation of esophageal reconstruction using the colon or the jejunum in esophageal cancer patients after gastrectomy. *Dis Esophagus.* 2008;21(2):132–8.
81. Cerfolio RJ, Allen MS, Deschamps C, Trastek VF, Pairolo PC. Esophageal replacement by colon interposition. *Ann Thorac Surg.* 1995;59(6):1382–4.
82. Briel JW, Tamhankar AP, Hagen JA, et al. Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. *J Am Coll Surg.* 2004;198(4):536–41. discussion 532–41.
83. Wain JC, Wright CD, Kuo EY, et al. Long-segment colon interposition for acquired esophageal disease. *Ann Thorac Surg.* 1999;67(2):313–7. discussion 317–8.
84. Ring WS, Varco RL, L'Heureux PR, Foker JE. Esophageal replacement with jejunum in children: an 18 to 33 year follow-up. *J Thorac Cardiovasc Surg.* 1982;83(6):918–27.
85. Smith RW, Garvey CJ, Dawson PM, Davies DM. Jejunum versus colon for free oesophageal reconstruction: an experimental radiological assessment. *Br J Plast Surg.* 1987;40(2):181–7.
86. Meyers WC, Seigler HF, Hanks JB, et al. Postoperative function of "free" jejunal transplants for replacement of the cervical esophagus. *Ann Surg.* 1980;192(4):439–50.
87. Wright C, Cuschieri A. Jejunal interposition for benign esophageal disease. Technical considerations and long-term results. *Ann Surg.* 1987;205(1):54–60.
88. Moreno-Oset E, Tomas-Ridocci M, Paris F, et al. Motor activity of esophageal substitute (stomach, jejunum, and colon segments). *Ann Thorac Surg.* 1986;41(5):515–9.
89. Swisher SG, Hofstetter WL, Miller MJ. The supercharged microvascular jejunal interposition. *Semin Thorac Cardiovasc Surg.* 2007;19(1):56–65.
90. Ascioti AJ, Hofstetter WL, Miller MJ, et al. Long-segment, supercharged, pedicled jejunal flap for total esophageal reconstruction. *J Thorac Cardiovasc Surg.* 2005;130(5):1391–8.
91. Sungurtekin H, Sungurtekin U, Balci C, Zencir M, Erdem E. The influence of nutritional status on complications after major intraabdominal surgery. *J Am Coll Nutr.* 2004;23(3):227–32.
92. Windsor JA, Hill GL. Weight loss with physiologic impairment. A basic indicator of surgical risk. *Ann Surg.* 1988;207(3):290–6.
93. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 2002 guidelines on perioperative cardiovascular evaluation for noncardiac surgery) developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *J Am Coll Cardiol.* 2007;50(17):1707–32.

94. Yamanaka Y, Mammoto T, Kita T, Kishi Y. A study of 13 patients with a gastric tube in place after esophageal resection: use of omeprazole to decrease gastric acidity and volume. *J Clin Anesth.* 2001;13(5):370–3.
95. Pisegna JR, Karlstadt RG, Norton JA, et al. Effect of preoperative intravenous pantoprazole in elective-surgery patients: a pilot study. *Dig Dis Sci.* 2009;54(5):1041–9.
96. Nishina K, Mikawa K, Takao Y, Shiga M, Maekawa N, Obara H. A comparison of rabeprazole, lansoprazole, and ranitidine for improving preoperative gastric fluid property in adults undergoing elective surgery. *Anesth Analg.* 2000;90(3):717–21.
97. Jeske HC, Borovicka J, von Goedecke A, et al. Preoperative administration of esomeprazole has no influence on frequency of refluxes. *J Clin Anesth.* 2008;20(3):191–5.
98. Ng A, Smith G. Gastroesophageal reflux and aspiration of gastric contents in anesthetic practice. *Anesth Analg.* 2001;93(2):494–513.
99. Pisegna JR, Martindale RG. Acid suppression in the perioperative period. *J Clin Gastroenterol.* 2005;39(1):10–6.
100. Rudin A, Flisberg P, Johansson J, Walther B, Lundberg CJ. Thoracic epidural analgesia or intravenous morphine analgesia after thoracoabdominal esophagectomy: a prospective follow-up of 201 patients. *J Cardiothorac Vasc Anesth.* 2005;19(3):350–7.
101. Flisberg P, Tornebrandt K, Walther B, Lundberg J. Pain relief after esophagectomy: thoracic epidural analgesia is better than parenteral opioids. *J Cardiothorac Vasc Anesth.* 2001;15(3):282–7.
102. Smedstad KG, Beattie WS, Blair WS, Buckley DN. Postoperative pain relief and hospital stay after total esophagectomy. *Clin J Pain.* 1992;8(2):149–53.
103. Tsui SL, Law S, Fok M, et al. Postoperative analgesia reduces mortality and morbidity after esophagectomy. *Am J Surg.* 1997;173(6):472–8.
104. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg.* 1998;86(3):598–612.
105. Cense HA, Lagarde SM, de Jong K, et al. Association of no epidural analgesia with postoperative morbidity and mortality after transthoracic esophageal cancer resection. *J Am Coll Surg.* 2006;202(3):395–400.
106. Michelet P, D'Journo XB, Roch A, et al. Perioperative risk factors for anastomotic leakage after esophagectomy: influence of thoracic epidural analgesia. *Chest.* 2005;128(5):3461–6.
107. Whooley BP, Law S, Murthy SC, Alexandrou A, Wong J. Analysis of reduced death and complication rates after esophageal resection. *Ann Surg.* 2001;233(3):338–44.
108. Yap FH, Lau JY, Joynt GM, Chui PT, Chan AC, Chung SS. Early extubation after transthoracic oesophagectomy. *Hong Kong Med J.* 2003;9(2):98–102.
109. Neal JM, Wilcox RT, Allen HW, Low DE. Near-total esophagectomy: the influence of standardized multimodal management and intraoperative fluid restriction. *Reg Anesth Pain Med.* 2003;28(4):328–34.
110. Low DE, Kunz S, Schembre D, et al. Esophagectomy – it's not just about mortality anymore: standardized perioperative clinical pathways improve outcomes in patients with esophageal cancer. *J Gastrointest Surg.* 2007;11(11):1395–402. discussion 1402.
111. Buise M, Van Bommel J, Mehra M, Tilanus HW, Van Zundert A, Gommers D. Pulmonary morbidity following esophagectomy is decreased after introduction of a multimodal anesthetic regimen. *Acta Anaesthesiol Belg.* 2008;59(4):257–61.
112. Kahn L, Baxter FJ, Dauphin A, et al. A comparison of thoracic and lumbar epidural techniques for post-thoracoabdominal esophagectomy analgesia. *Can J Anaesth.* 1999;46(5 Pt 1):415–22.
113. Luketich JD, Land SR, Sullivan EA, et al. Thoracic epidural versus intercostal nerve catheter plus patient-controlled analgesia: a randomized study. *Ann Thorac Surg.* 2005;79(6):1845–9. discussion 1849–50.
114. Debreceni G, Molnar Z, Szelig L, Molnar TF. Continuous epidural or intercostal analgesia following thoracotomy: a prospective randomized double-blind clinical trial. *Acta Anaesthesiol Scand.* 2003;47(9):1091–5.
115. Francois T, Blanloel Y, Pillet F, et al. Effect of interpleural administration of bupivacaine or lidocaine on pain and morphine requirement after esophagectomy with thoracotomy: a randomized, double-blind and controlled study. *Anesth Analg.* 1995;80(4):718–23.
116. Wheatley III GH, Rosenbaum DH, Paul MC, et al. Improved pain management outcomes with continuous infusion of a local anesthetic after thoracotomy. *J Thorac Cardiovasc Surg.* 2005;130(2):464–8.
117. Marret E, Bazelly B, Taylor G, et al. Paravertebral block with ropivacaine 0.5% versus systemic analgesia for pain relief after thoracotomy. *Ann Thorac Surg.* 2005;79(6):2109–13.
118. Casati A, Alessandrini P, Nuzzi M, et al. A prospective, randomized, blinded comparison between continuous thoracic paravertebral and epidural infusion of 0.2% ropivacaine after lung resection surgery. *Eur J Anaesthesiol.* 2006;23(12):999–1004.
119. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy – a systematic review and meta-analysis of randomized trials. *Br J Anaesth.* 2006;96(4):418–26.
120. Conlon NP, Shaw AD, Grichnik KP. Postthoracotomy paravertebral analgesia: will it replace epidural analgesia? *Anesthesiol Clin.* 2008;26(2):369–80, viii.
121. Daly DJ, Myles PS. Update on the role of paravertebral blocks for thoracic surgery: are they worth it? *Curr Opin Anaesthesiol.* 2009;22(1):38–43.
122. Yegin A, Erdogan A, Kayacan N, Karsli B. Early postoperative pain management after thoracic surgery; pre- and postoperative versus postoperative epidural analgesia: a randomised study. *Eur J Cardiothorac Surg.* 2003;24(3):420–4.
123. Bong CL, Samuel M, Ng JM, Ip-Yam C. Effects of preemptive epidural analgesia on post-thoracotomy pain. *J Cardiothorac Vasc Anesth.* 2005;19(6):786–93.
124. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain.* 1996;12(1):50–5.
125. Chen HC, Huang HJ, Wu CY, Lin TS, Fang HY. Esophageal schwannoma with tracheal compression. *Thorac Cardiovasc Surg.* 2006;54(8):555–8.
126. Mizuguchi S, Inoue K, Imagawa A, et al. Benign esophageal schwannoma compressing the trachea in pregnancy. *Ann Thorac Surg.* 2008;85(2):660–2.
127. Sasano H, Sasano N, Ito S, et al. Continuous positive airway pressure applied through a bronchial blocker as a treatment for hypoxemia due to stenosis of the left main bronchus. *Anesthesiology.* 2009;110(5):1199–200.
128. Andronikou S, Wieselthaler N, Kilborn T. Significant airway compromise in a child with a posterior mediastinal mass due to tuberculous spondylitis. *Pediatr Radiol.* 2005;35(11):1159–60.

129. Blank RS, Waldrop CS, Balestrieri PJ. Pseudomeningocele: an unusual cause of intraoperative tracheal compression and expiratory obstruction. *Anesth Analg.* 2008;107(1):226–8.
130. ul Huda A, Siddiqui KM, Khan FH. Emergency airway management of a patient with mediastinal mass. *J Pak Med Assoc.* 2007;57(3):152–4.
131. Tokunaga T, Takeda S, Sumimura J, Maeda H. Esophageal schwannoma: report of a case. *Surg Today.* 2007;37(6):500–2.
132. Hasan N, Mandhan P. Respiratory obstruction caused by lipoma of the esophagus. *J Pediatr Surg.* 1994;29(12):1565–6.
133. Arcos E, Medina C, Mearin F, Larish J, Guarner L, Malagelada JR. Achalasia presenting as acute airway obstruction. *Dig Dis Sci.* 2000;45(10):2079–83.
134. Bechard P, Letourneau L, Lacasse Y, Cote D, Bussieres JS. Perioperative cardiorespiratory complications in adults with mediastinal mass: incidence and risk factors. *Anesthesiology.* 2004;100(4):826–34. discussion 825A.
135. Black DR, Thangathurai D, Senthilkumar N, Roffey P, Mikhail M. High risk of aspiration and difficult intubation in post-esophagectomy patients. *Acta Anaesthesiol Scand.* 1999;43(6):687.
136. Pennefather SH. Anaesthesia for oesophagectomy. *Curr Opin Anaesthesiol.* 2007;20(1):15–20.
137. Ng JM. Perioperative anesthetic management for esophagectomy. *Anesthesiol Clin.* 2008;26(2):293–304, vi.
138. de Souza DG, Gaughen CL. Aspiration risk after esophagectomy. *Anesth Analg.* 2009;109(4):1352.
139. Robinson GV, Kanji H, Davies RJ, Gleeson FV. Selective pulmonary fat aspiration complicating oesophageal achalasia. *Thorax.* 2004;59(2):180.
140. Akritidis N, Gousis C, Dimos G, Paparounas K. Fever, cough, and bilateral lung infiltrates. Achalasia associated with aspiration pneumonia. *Chest.* 2003;123(2):608–12.
141. American Society of Anesthesiologist Task Force on Preoperative Fasting. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: a report by the American Society of Anesthesiologist Task Force on Preoperative Fasting. *Anesthesiology.* 1999;90(3):896–905.
142. Brady M, Kinn S, Stuart P. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev.* 2003;4:CD004423.
143. Ovassapian A, Salem MR. Sellick's maneuver: to do or not do. *Anesth Analg.* 2009;109(5):1360–2.
144. Lerman J. On cricoid pressure: “may the force be with you”. *Anesth Analg.* 2009;109(5):1363–6.
145. Smith KJ, Dobranowski J, Yip G, Dauphin A, Choi PT. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology.* 2003;99(1):60–4.
146. Rice MJ, Mancuso AA, Gibbs C, Morey TE, Gravenstein N, Deitte LA. Cricoid pressure results in compression of the post-cricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg.* 2009;109(5):1546–52.
147. Brimacombe JR, Berry AM. Cricoid pressure. *Can J Anaesth.* 1997;44(4):414–25.
148. Ellis DY, Harris T, Zideman D. Cricoid pressure in emergency department rapid sequence tracheal intubations: a risk-benefit analysis. *Ann Emerg Med.* 2007;50(6):653–65.
149. Heath KJ, Palmer M, Fletcher SJ. Fracture of the cricoid cartilage after Sellick's manoeuvre. *Br J Anaesth.* 1996;76(6):877–8.
150. Landsman I. Cricoid pressure: indications and complications. *Paediatr Anaesth.* 2004;14(1):43–7.
151. Garrard A, Campbell AE, Turley A, Hall JE. The effect of mechanically-induced cricoid force on lower oesophageal sphincter pressure in anaesthetised patients. *Anaesthesia.* 2004;59(5):435–9.
152. Whittington RM, Robinson JS, Thompson JM. Prevention of fatal aspiration syndrome. *Lancet.* 1979;2(8143):630–1.
153. Williamson R. Cricoid pressure. *Can J Anaesth.* 1989;36(5):601.
154. Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth.* 2007;54(9):748–64.
155. Gobindram A, Clarke S. Cricoid pressure: should we lay off the pressure? *Anaesthesia.* 2008;63(11):1258–9.
156. Snow RG, Nunn JF. Induction of anaesthesia in the foot-down position for patients with a full stomach. *Br J Anaesth.* 1959;31:493–7.
157. Hodges RJ, Bennett JR, Tunstall ME, Knight RF. General anaesthesia for operative obstetrics: with special reference to the use of thiopentone and suxamethonium. *Br J Anaesth.* 1959;31(4):152–63.
158. Agnew NM, Kendall JB, Akrofi M, et al. Gastroesophageal reflux and tracheal aspiration in the thoracotomy position: should ranitidine premedication be routine? *Anesth Analg.* 2002;95(6):1645–9.
159. Blunt MC, Young PJ, Patil A, Haddock A. Gel lubrication of the tracheal tube cuff reduces pulmonary aspiration. *Anesthesiology.* 2001;95(2):377–81.
160. Sanjay PS, Miller SA, Corry PR, Russell GN, Pennefather SH. The effect of gel lubrication on cuff leakage of double lumen tubes during thoracic surgery. *Anaesthesia.* 2006;61(2):133–7.
161. Shackcloth MJ, McCarron E, Kendall J, et al. Randomized clinical trial to determine the effect of nasogastric drainage on tracheal acid aspiration following oesophagectomy. *Br J Surg.* 2006;93(5):547–52.
162. Benumof JL. Difficult tubes and difficult airways. *J Cardiothorac Vasc Anesth.* 1998;12(2):131–2.
163. Vanner R. Arndt endobronchial blocker during oesophagectomy. *Anaesthesia.* 2005;60(3):295–6.
164. Chen A, Lai HY, Lin PC, Chen TY, Shyr MH. GlideScope-assisted double-lumen endobronchial tube placement in a patient with an unanticipated difficult airway. *J Cardiothorac Vasc Anesth.* 2008;22(1):170–2.
165. Yamazaki T, Ohsumi H. The airway scope is a practical intubation device for a double-lumen tube during rapid-sequence induction. *J Cardiothorac Vasc Anesth.* 2009;23(6):926.
166. Angie Ho CY, Chen CY, Yang MW, Liu HP. Use of the Arndt wire-guided endobronchial blocker via nasal for one-lung ventilation in patient with anticipated restricted mouth opening for esophagectomy. *Eur J Cardiothorac Surg.* 2005;28(1):174–5.
167. Narayanaswamy M, McRae K, Slinger P, et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. *Anesth Analg.* 2009;108(4):1097–101.
168. Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M. A rational approach to perioperative fluid management. *Anesthesiology.* 2008;109(4):723–40.

169. Holte K, Sharrock NE, Kehlet H. Pathophysiology and clinical implications of perioperative fluid excess. *Br J Anaesth.* 2002; 89(4):622–32.
170. Brandstrup B, Tonnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg.* 2003;238(5):641–8.
171. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet.* 2002;359(9320):1812–8.
172. Nisanovich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology.* 2005;103(1):25–32.
173. Bernard A, Deschamps C, Allen MS, et al. Pneumonectomy for malignant disease: factors affecting early morbidity and mortality. *J Thorac Cardiovasc Surg.* 2001;121(6):1076–82.
174. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97(6):1558–65.
175. Fernandez-Perez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology.* 2006;105(1):14–8.
176. Wei S, Tian J, Song X, Chen Y. Association of perioperative fluid balance and adverse surgical outcomes in esophageal cancer and esophagogastric junction cancer. *Ann Thorac Surg.* 2008;86(1):266–72.
177. Kita T, Mammoto T, Kishi Y. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. *J Clin Anesth.* 2002;14(4):252–6.
178. Concha MR, Mertz VF, Cortinez LI, et al. The volume of lactated Ringer's solution required to maintain preload and cardiac index during open and laparoscopic surgery. *Anesth Analg.* 2009;108(2):616–22.
179. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest.* 2008;134(1):172–8.
180. Oohashi S, Endoh H. Does central venous pressure or pulmonary capillary wedge pressure reflect the status of circulating blood volume in patients after extended transthoracic esophagectomy? *J Anesth.* 2005;19(1):21–5.
181. Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology.* 2002;97(4):820–6.
182. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445]. *Crit Care.* 2005;9(6):R687–93.
183. Donati A, Loggi S, Preiser JC, et al. Goal-directed intraoperative therapy reduces morbidity and length of hospital stay in high-risk surgical patients. *Chest.* 2007;132(6):1817–24.
184. Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler Jr JO, Michard F. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care.* 2007;11(5):R100.
185. Noblett SE, Snowden CP, Shenton BK, Horgan AF. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. *Br J Surg.* 2006;93(9):1069–76.
186. Mythen MG, Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. *Arch Surg.* 1995;130(4):423–9.
187. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. *BMJ.* 1997;315(7113):909–12.
188. McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomised controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimisation of circulatory status after cardiac surgery. *BMJ.* 2004;329(7460):258.
189. Wakeling HG, McFall MR, Jenkins CS, et al. Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *Br J Anaesth.* 2005;95(5):634–42.
190. Goepfert MS, Reuter DA, Akyol D, Lamm P, Kilger E, Goetz AE. Goal-directed fluid management reduces vasopressor and catecholamine use in cardiac surgery patients. *Intensive Care Med.* 2007;33(1):96–103.
191. Bundgaard-Nielsen M, Holte K, Secher NH, Kehlet H. Monitoring of peri-operative fluid administration by individualized goal-directed therapy. *Acta Anaesthesiol Scand.* 2007;51(3):331–40.
192. Manecke GR. Edwards FloTrac sensor and Vigileo monitor: easy, accurate, reliable cardiac output assessment using the arterial pulse wave. *Expert Rev Med Devices.* 2005;2(5):523–7.
193. Cannesson M, Musard H, Desebbe O, et al. The ability of stroke volume variations obtained with Vigileo/FloTrac system to monitor fluid responsiveness in mechanically ventilated patients. *Anesth Analg.* 2009;108(2):513–7.
194. Manecke Jr GR, Auger WR. Cardiac output determination from the arterial pressure wave: clinical testing of a novel algorithm that does not require calibration. *J Cardiothorac Vasc Anesth.* 2007;21(1):3–7.
195. Godje O, Hoke K, Goetz AE, et al. Reliability of a new algorithm for continuous cardiac output determination by pulse-contour analysis during hemodynamic instability. *Crit Care Med.* 2002;30(1):52–8.
196. Moretti EW, Robertson KM, El-Moalem H, Gan TJ. Intraoperative colloid administration reduces postoperative nausea and vomiting and improves postoperative outcomes compared with crystalloid administration. *Anesth Analg.* 2003;96(2):611–7.
197. Kimberger O, Arnberger M, Brandt S, et al. Goal-directed colloid administration improves the microcirculation of healthy and perianastomotic colon. *Anesthesiology.* 2009;110(3):496–504.
198. Lang K, Boldt J, Suttner S, Haisch G. Colloids versus crystalloids and tissue oxygen tension in patients undergoing major abdominal surgery. *Anesth Analg.* 2001;93(2):405–9.
199. McIlroy DR, Kharasch ED. Acute intravascular volume expansion with rapidly administered crystalloid or colloid in the setting of moderate hypovolemia. *Anesth Analg.* 2003;96(6):1572–7.
200. Di Filippo A, Ciapetti M, Prencipe D, et al. Experimentally-induced acute lung injury: the protective effect of hydroxyethyl starch. *Ann Clin Lab Sci.* 2006;36(3):345–52.
201. Verheij J, van Lingen A, Raijmakers PG, et al. Effect of fluid loading with saline or colloids on pulmonary permeability, oedema and lung injury score after cardiac and major vascular surgery. *Br J Anaesth.* 2006;96(1):21–30.
202. Matharu NM, Butler LM, Rainger GE, Gosling P, Vohra RK, Nash GB. Mechanisms of the anti-inflammatory effects of hydroxyethyl starch demonstrated in a flow-based model of

- neutrophil recruitment by endothelial cells. *Crit Care Med.* 2008;36(5):1536–42.
203. Boldt J, Brosch C, Rohm K, Lehmann A, Mengistu A, Suttorp S. Is albumin administration in hypoalbuminemic elderly cardiac surgery patients of benefit with regard to inflammation, endothelial activation, and long-term kidney function? *Anesth Analg.* 2008;107(5):1496–503.
204. Jacob M, Bruegger D, Rehm M, Welsch U, Conzen P, Becker BF. Contrasting effects of colloid and crystalloid resuscitation fluids on cardiac vascular permeability. *Anesthesiology.* 2006;104(6):1223–31.
205. Rackow EC, Weil MH, Macneil AR, Makabali CG, Michaels S. Effects of crystalloid and colloid fluids on extravascular lung water in hypoproteinemic dogs. *J Appl Physiol.* 1987;62(6):2421–5.
206. Nohe B, Burchard M, Zanke C, et al. Endothelial accumulation of hydroxyethyl starch and functional consequences on leukocyte-endothelial interactions. *Eur Surg Res.* 2002;34(5):364–72.
207. Nohe B, Johannes T, Reutershans J, et al. Synthetic colloids attenuate leukocyte-endothelial interactions by inhibition of integrin function. *Anesthesiology.* 2005;103(4):759–67.
208. Handrigan MT, Burns AR, Donnachie EM, Bowden RA. Hydroxyethyl starch inhibits neutrophil adhesion and transendothelial migration. *Shock.* 2005;24(5):434–9.
209. Rehm M, Zahler S, Lotsch M, et al. Endothelial glycocalyx as an additional barrier determining extravasation of 6% hydroxyethyl starch or 5% albumin solutions in the coronary vascular bed. *Anesthesiology.* 2004;100(5):1211–23.
210. Jungheinrich C, Scharpf R, Wargenau M, Bepperling F, Baron JF. The pharmacokinetics and tolerability of an intravenous infusion of the new hydroxyethyl starch 130/0.4 (6%, 500 mL) in mild-to-severe renal impairment. *Anesth Analg.* 2002;95(3):544–51.
211. Boldt J, Brosch C, Ducke M, Papsdorf M, Lehmann A. Influence of volume therapy with a modern hydroxyethylstarch preparation on kidney function in cardiac surgery patients with compromised renal function: a comparison with human albumin. *Crit Care Med.* 2007;35(12):2740–6.
212. Mukhtar A, Aboulfetouh F, Obayah G, et al. The safety of modern hydroxyethyl starch in living donor liver transplantation: a comparison with human albumin. *Anesth Analg.* 2009;109(3):924–30.
213. Gandhi SD, Weiskopf RB, Jungheinrich C, et al. Volume replacement therapy during major orthopedic surgery using Voluven (hydroxyethyl starch 130/0.4) or hetastarch. *Anesthesiology.* 2007;106(6):1120–7.
214. Gallandat Huet RC, Siemons AW, Baus D, et al. A novel hydroxyethyl starch (Voluven) for effective perioperative plasma volume substitution in cardiac surgery. *Can J Anaesth.* 2000;47(12):1207–15.
215. Boldt J, Ducke M, Kumle B, Papsdorf M, Zurmeyer EL. Influence of different volume replacement strategies on inflammation and endothelial activation in the elderly undergoing major abdominal surgery. *Intensive Care Med.* 2004;30(3):416–22.
216. Faulx AL, Catanzaro A, Zyzanski S, et al. Patient tolerance and acceptance of unsedated ultrathin esophagoscopy. *Gastrointest Endosc.* 2002;55(6):620–3.
217. Nguyen ST, Cabrales RE, Bashour CA, et al. Benzocaine-induced methemoglobinemia. *Anesth Analg.* 2000;90(2):369–71.
218. Gunaratnam NT, Vazquez-Sequeiros E, Gostout CJ, Alexander GL. Methemoglobinemia related to topical benzocaine use: is it time to reconsider the empiric use of topical anesthesia before sedated EGD? *Gastrointest Endosc.* 2000;52(5):692–3.
219. Busick T, Kussman M, Scheidt T, Tobias JD. Preliminary experience with dexmedetomidine for monitored anesthesia care during ENT surgical procedures. *Am J Ther.* 2008;15(6):520–7.
220. Gitzelmann CA, Gysin C, Weiss M. Dorsal flexion of head and neck for rigid oesophagoscopy – a caution for hidden foreign bodies dropped into the epipharynx. *Acta Anaesthesiol Scand.* 2003;47(9):1178–9.
221. Lee SH. The role of oesophageal stenting in the non-surgical management of oesophageal strictures. *Br J Radiol.* 2001;74(886):891–900.
222. Verschuur EM, Kuipers EJ, Siersema PD. Esophageal stents for malignant strictures close to the upper esophageal sphincter. *Gastrointest Endosc.* 2007;66(6):1082–90.
223. Freeman RK, Van Woerkom JM, Ascoti AJ. Esophageal stent placement for the treatment of iatrogenic intrathoracic esophageal perforation. *Ann Thorac Surg.* 2007;83(6):2003–7. discussion 2007–8.
224. Annese V, Bassotti G. Non-surgical treatment of esophageal achalasia. *World J Gastroenterol.* 2006;12(36):5763–6.
225. Calverley RK, Johnston AE. The anaesthetic management of tracheo-oesophageal fistula: a review of ten years' experience. *Can Anaesth Soc J.* 1972;19(3):270–82.
226. Baraka A, Slim M. Cardiac arrest during IPPV in a newborn with tracheoesophageal fistula. *Anesthesiology.* 1970;32(6):564–5.
227. Horishita T, Ogata J, Minami K. Unique anaesthetic management of a patient with a large tracheoesophageal fistula using fiberoptic bronchoscopy. *Anesth Analg.* 2003;97(6):1856.
228. Chan CS. Anaesthetic management during repair of tracheo-oesophageal fistula. *Anaesthesia.* 1984;39(2):158–60.
229. Ichinose M, Sakai H, Miyazaki I, et al. Independent lung ventilation combined with HFOV for a patient suffering from tracheo-gastric roll fistula. *J Anesth.* 2008;22(3):282–5.
230. Patti MG, Wiener-Kronish JP, Way LW, Pellegrini CA. Impact of transhiatal esophagectomy on cardiac and respiratory function. *Am J Surg.* 1991;162(6):563–6. discussion 566–7.
231. Malhotra SK, Kaur RP, Gupta NM, Grover A, Ramprabu K, Nakra D. Incidence and types of arrhythmias after mediastinal manipulation during transhiatal esophagectomy. *Ann Thorac Surg.* 2006;82(1):298–302.
232. Ikeda Y, Niimi M, Kan S, Shatari T, Takami H, Kodaira S. Clinical significance of tissue blood flow during esophagectomy by laser Doppler flowmetry. *J Thorac Cardiovasc Surg.* 2001;122(6):1101–6.
233. Kusano C, Baba M, Takao S, et al. Oxygen delivery as a factor in the development of fatal postoperative complications after oesophagectomy. *Br J Surg.* 1997;84(2):252–7.
234. Urschel JD. Esophagogastronomy anastomotic leaks complicating esophagectomy: a review. *Am J Surg.* 1995;169(6):634–40.
235. Al-Rawi OY, Pennefather SH, Page RD, Dave I, Russell GN. The effect of thoracic epidural bupivacaine and an intravenous adrenaline infusion on gastric tube blood flow during esophagectomy. *Anesth Analg.* 2008;106(3):884–7.
236. Page RD, Shackcloth MJ, Russell GN, Pennefather SH. Surgical treatment of anastomotic leaks after oesophagectomy. *Eur J Cardiothorac Surg.* 2005;27(2):337–43.
237. Bartels H, Stein HJ, Siewert JR. Early extubation vs. late extubation after esophagus resection: a randomized, prospective study. *Langenbecks Arch Chir Suppl Kongressbd.* 1998;115:1074–6.

238. Caldwell MT, Murphy PG, Page R, Walsh TN, Hennessy TP. Timing of extubation after oesophagectomy. *Br J Surg.* 1993;80(12):1537–9.
239. Lanuti M, de Delva PE, Maher A, et al. Feasibility and outcomes of an early extubation policy after esophagectomy. *Ann Thorac Surg.* 2006;82(6):2037–41.
240. Jiang K, Cheng L, Wang JJ, Li JS, Nie J. Fast track clinical pathway implications in esophagogastrectomy. *World J Gastroenterol.* 2009;15(4):496–501.
241. Chandrashekhar MV, Irving M, Wayman J, Raimes SA, Linsley A. Immediate extubation and epidural analgesia allow safe management in a high-dependency unit after two-stage oesophagectomy. Results of eight years of experience in a specialized upper gastrointestinal unit in a district general hospital. *Br J Anaesth.* 2003;90(4):474–9.
242. Verhage RJ, Hazebroek EJ, Boone J, Van Hillegersberg R. Minimally invasive surgery compared to open procedures in esophagectomy for cancer: a systematic review of the literature. *Minerva Chir.* 2009;64(2):135–46.
243. Martin LW, Hofstetter W, Swisher SG, Roth JA. Management of intrathoracic leaks following esophagectomy. *Adv Surg.* 2006;40:173–90.
244. Amar D, Burt ME, Bains MS, Leung DH. Symptomatic tachyarrhythmias after esophagectomy: incidence and outcome measures. *Ann Thorac Surg.* 1996;61(5):1506–9.
245. Murthy SC, Law S, Whooley BP, Alexandrou A, Chu KM, Wong J. Atrial fibrillation after esophagectomy is a marker for postoperative morbidity and mortality. *J Thorac Cardiovasc Surg.* 2003;126(4):1162–7.
246. Vaporiyan AA, Correa AM, Rice DC, et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. *J Thorac Cardiovasc Surg.* 2004;127(3):779–86.
247. Ma JY, Wang Y, Zhao YF, et al. Atrial fibrillation after surgery for esophageal carcinoma: clinical and prognostic significance. *World J Gastroenterol.* 2006;12(3):449–52.
248. Sedrakyan A, Treasure T, Browne J, Krumholz H, Sharpin C, van der Meulen J. Pharmacologic prophylaxis for postoperative atrial tachyarrhythmia in general thoracic surgery: evidence from randomized clinical trials. *J Thorac Cardiovasc Surg.* 2005;129(5):997–1005.
249. Law SY, Fok M, Wong J. Risk analysis in resection of squamous cell carcinoma of the esophagus. *World J Surg.* 1994;18(3):339–46.
250. Law S, Wong KH, Kwok KF, Chu KM, Wong J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. *Ann Surg.* 2004;240(5):791–800.
251. Ferguson MK, Durkin AE. Preoperative prediction of the risk of pulmonary complications after esophagectomy for cancer. *J Thorac Cardiovasc Surg.* 2002;123(4):661–9.
252. Bailey SH, Bull DA, Harpole DH, et al. Outcomes after esophagectomy: a ten-year prospective cohort. *Ann Thorac Surg.* 2003;75(1):217–22, discussion 222.
253. Muller JM, Erasmi H, Stelzner M, Zieren U, Pichlmaier H. Surgical therapy of oesophageal carcinoma. *Br J Surg.* 1990;77(8):845–57.
254. Jiao WJ, Wang TY, Gong M, Pan H, Liu YB, Liu ZH. Pulmonary complications in patients with chronic obstructive pulmonary disease following transthoracic esophagectomy. *World J Gastroenterol.* 2006;12(16):2505–9.
255. Tandon S, Batchelor A, Bullock R, et al. Peri-operative risk factors for acute lung injury after elective oesophagectomy. *Br J Anaesth.* 2001;86(5):633–8.
256. Michelet P, D'Journo XB, Roch A, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology.* 2006;105(5):911–9.
257. Nakanishi K, Takeda S, Terajima K, Takano T, Ogawa R. Myocardial dysfunction associated with proinflammatory cytokines after esophageal resection. *Anesth Analg.* 2000;91(2):270–5.
258. Kooguchi K, Kobayashi A, Kitamura Y, et al. Elevated expression of inducible nitric oxide synthase and inflammatory cytokines in the alveolar macrophages after esophagectomy. *Crit Care Med.* 2002;30(1):71–6.
259. Reid PT, Donnelly SC, MacGregor IR, et al. Pulmonary endothelial permeability and circulating neutrophil-endothelial markers in patients undergoing esophagogastrectomy. *Crit Care Med.* 2000;28(9):3161–5.
260. Rocker GM, Wiseman MS, Pearson D, Shale DJ. Neutrophil degranulation and increased pulmonary capillary permeability following oesophagectomy: a model of early lung injury in man. *Br J Surg.* 1988;75(9):883–6.
261. Donnelly SC, Strieter RM, Kunkel SL, et al. Interleukin-8 and development of adult respiratory distress syndrome in at-risk patient groups. *Lancet.* 1993;341(8846):643–7.
262. Hay DW, Sarau HM. Interleukin-8 receptor antagonists in pulmonary diseases. *Curr Opin Pharmacol.* 2001;1(3):242–7.
263. Zeilhofer HU, Schorr W. Role of interleukin-8 in neutrophil signaling. *Curr Opin Hematol.* 2000;7(3):178–82.
264. Cree RT, Warnell I, Staunton M, et al. Alveolar and plasma concentrations of interleukin-8 and vascular endothelial growth factor following oesophagectomy. *Anaesthesia.* 2004;59(9):867–71.
265. Tsukada K, Hasegawa T, Miyazaki T, et al. Predictive value of interleukin-8 and granulocyte elastase in pulmonary complication after esophagectomy. *Am J Surg.* 2001;181(2):167–71.
266. Michelet P, Roch A, D'Journo XB, et al. Effect of thoracic epidural analgesia on gastric blood flow after oesophagectomy. *Acta Anaesthesiol Scand.* 2007;51(5):587–94.
267. Lazar G, Kaszaki J, Abraham S, et al. Thoracic epidural anesthesia improves the gastric microcirculation during experimental gastric tube formation. *Surgery.* 2003;134(5):799–805.
268. Tsai JA, Lund M, Lundell L, Nilsson-Ekdahl K. One-lung ventilation during thoracoabdominal esophagectomy elicits complement activation. *J Surg Res.* 2009;152(2):331–7.
269. Terragni PP, Del Sorbo L, Mascia L, et al. Tidal volume lower than 6 ml/kg enhances lung protection: role of extracorporeal carbon dioxide removal. *Anesthesiology.* 2009;111(4):826–35.
270. Oda K, Akiyama S, Ito K, et al. Perioperative prostaglandin E1 treatment for the prevention of postoperative complications after esophagectomy: a randomized clinical trial. *Surg Today.* 2004;34(8):662–7.
271. Matsuzaki Y, Edagawa M, Maeda M, et al. Beneficial effect of prostaglandin E1 on blood flow to the gastric tube after esophagectomy. *Ann Thorac Surg.* 1999;67(4):908–10.
272. Hasegawa S, Imamura M, Shimada Y, et al. Prostaglandin E1 ameliorates decreased tracheal blood flow after esophagectomy and aggressive upper mediastinal lymphadenectomy for esophageal carcinoma. *J Am Coll Surg.* 1996;183(4):371–6.
273. Schneemilch CE, Schilling T, Bank U. Effects of general anaesthesia on inflammation. *Best Pract Res Clin Anaesthesiol.* 2004;18(3):493–507.
274. De Conno E, Steurer MP, Wittlinger M, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *Anesthesiology.* 2009;110(6):1316–26.

31

Anesthesia for Robotic Thoracic Surgery

Javier Campos

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Key Points

- The management of the robotic thoracic surgical patient requires the knowledge of minimally invasive surgery techniques involving the chest.
- Familiarity with the da Vinci® robot surgical system by the anesthesiologist is mandatory.
- Management of one-lung ventilation techniques with a left-sided double-lumen endotracheal tube or an independent bronchial blocker is required, along with flexible fiberoptic bronchoscopy techniques.
- Patient positioning and prevention of complications such as nerve or crashing injuries while the robotic system is used.
- Recognition of the hemodynamic effects of carbon dioxide (CO₂) during insufflation in the chest is required.
- Potential for conversion to open thoracotomy or open procedure in the abdomen.

Introduction

Minimally invasive surgery approaches have become increasingly popular in cardiac, thoracic, and esophageal surgery [1–5]. With the introduction of robotic systems, specifically the da Vinci® robot surgical system, more than 10 years ago, a wide variety of surgical operations have been performed with some provocative results and limited defined advantages. This chapter provides an overview of the anesthetic implications and the use of the robotic system in patients undergoing mediastinal mass resection, pulmonary resections, and esophageal surgery.

The da Vinci® Robot Surgical System

The da Vinci® robot surgical system provides three dimensional (3D) video imaging plus a set of telemanipulated flexible effector instruments [6]. The system consists of three major components, a console for the operating surgeon, a patient-side cart with four interactive robotic arms, and a vision cart including optical devices for the robotic camera [7]. Figure 31.1 displays the da Vinci® robot surgical system.

In brief the surgeon operates while seated at a console and views a 3D image of the surgical fields through the vision system. The patient-side cart (the actual robot) consists of three or four robotic arms, two or three instrument arms, and one endoscope arm which houses the camera. A full range of EndoWrists (Surgical Intuitive) instruments are used to assist with the surgery. These EndoWrists provide seven degrees of motion which exceeds the capacity of a surgeon's hand in open surgery and two degrees of axial rotation to replicate human wrist-like movements. In clinical practice the first two arms, representing the surgeon's left and right hands, hold the EndoWrist instruments; a third arm positions the endoscope, the optional fourth arm, which represent the latest design in the da Vinci® robot surgical system, adds surgical capabilities by enabling the surgeon to add a third EndoWrist instrument. The surgical instruments are introduced via special ports and attached to the arms of the robot. The surgeon sitting at the console triggers highly sensitive motion sensors that transfer the surgeon's movement to the tip of the instruments. Figure 31.2 displays the console and a surgeon seated and performing robotic surgery. Figure 31.3 displays the Endo Wrist instruments during a thoracic surgical case.



FIG. 31.1. Displays (a) the console (b) a three arm da Vinci® robot surgical system and (c) video monitor.



FIG. 31.2. Displays the console and a surgeon seated and performing robotic surgery.



FIG. 31.3. Displays the Endo Wrist instruments during a thoracic surgical case.

TABLE 31.1. Advantages and disadvantages of robotic thoracic surgery.

Advantages of robotic thoracic surgery

- Shorter hospital length of stay
- Less pain
- Less blood loss and need for transfusion
- Minimal scarring
- Faster recovery
- Faster return to normal activities

Disadvantages

- Increasing surgical times
- Increased number of operating room personnel needed
- Potential for conversion to open procedure
- Cost and outcomes (need to be compared with other techniques)

TABLE 31.2. Surgical procedures performed in thoracic surgery with the da Vinci® robotic surgical system.

- Thymectomy
- Mediastinal mass resection
- Nissen fundoplications
- Esophageal dissections
- Esophagectomy
- Pulmonary lobectomy

Robotic surgical procedures are usually performed by two surgeons, the surgeon at the console and the table-side surgeon, who introduces the trocars and connects them with the robotic arms and changes the robotic instruments through the other ports if needed. The size of the robotic trocar is 10 mm for the binocular robotic camera and 8 mm for the instruments. Some of the potential advantages of using a robotic surgical system in thoracic surgery include: shorter hospital length of stay, less pain, less blood loss and transfusion, minimal scarring, faster recovery, and probably a faster return to normal activities [8, 9]. Table 31.1 displays the advantages and disadvantages of robotic thoracic surgery. Table 31.2 displays the surgical procedures performed in thoracic surgery with the da Vinci® robot surgical system.

Anesthetic Implications in Robotic Thoracic Surgery

The basic principles applied to minimally invasive surgery of the chest (i.e., thoracoscopic surgery, see also Chap. 23) also apply to robotic-assisted thoracic surgery. The combination of patient position, management of one-lung ventilation (OLV) techniques, and surgical manipulations alter ventilation and perfusion from the dependant and nondependant or collapsed lung. The preferred method for lung isolation during robotic-assisted thoracic surgery is the use of a left-sided double-lumen endotracheal tube (DLT) because of the greater margin of safety and faster and more reliable lung collapse. Also, it provides ready access for bronchoscopic evaluation of the airway during surgical resection.

In general, careful attention must be given to airway devices because changes in body position may cause tube migration. OLV anesthetic management is more challenging during robotic thoracic surgery due to the presence of the robot chassis that is stationed over the patient. The patient's airway is also usually located far from the anesthesia field. In some instances access to the airway, if needed, is not optimal because of the presence of the robotic arms nearby. In addition, visualization during robotic thoracic surgery may be enhanced by continuous intrathoracic carbon dioxide (CO_2) insufflation, which may increase airway pressures. When CO_2 is used it should not exceed intrathoracic pressures of 10–15 mmHg. Increasing the intrathoracic pressure (i.e., >25 mmHg) can compromise venous return and cardiac compliance; also the dependant lung develops higher airway pressures and ventilation can become difficult. During the surgical procedure, the FiO_2 should be maintained at 100% and the peak inspiratory pressure should be kept <30 cm H_2O . The ventilatory parameters should be adjusted to maintain a PaCO_2 at approximately 40 mmHg.

Robotic-Assisted Surgery and Anesthesia for Mediastinal Masses

Among the thoracic surgical procedures performed to date with the use of the da Vinci® robot surgical system is thymectomy [3]. Of the patients scheduled for robotic-assisted thymectomy, some have the diagnosis of myasthenia gravis because of the presence of a thymoma. Preparation of the patient for surgery includes neurological evaluation to assess the patient's neurological status and optimization of neurological conditions; continuation of anticholinesterase therapy and plasmapheresis may be indicated in some cases [10, 11] (see also Chap. 15). Precautions regarding anesthetic management include the proper dosing of muscle relaxants and the potential consequences of a large mediastinal mass on oxygenation and ventilation.

Positioning the patient for a thymectomy with the use of the robot system requires an optimal surgical position. In these cases, the patients are placed in an incomplete side-up position at a 30° angle right or a left lateral decubitus position with the use of a beanbag. The arm of the elevated side is positioned at the patient's side as far back as possible so the surgeon can gain enough space for the robotic arms. While the robot is in use it is imperative to consider strategies to protect all pressure points and to avoid unnecessary stretching of the elevated arm because this can cause damage to the brachial plexus. Also, because the arm of the robot is in the chest cavity, a complete lung collapse must be maintained throughout the procedure. Robotic surgery with the da Vinci® robot surgical system does not allow for changes in patient position on the operating room table once the robot has been docked. Robotic thymectomy requires that the operating room table be rotated 90° away from the anesthesiologist's field. For this reason access to the airway to make adjustments

to the DLT during the surgery can be challenging. In some cases, a bilateral approach may be required. In these cases, the operation is performed in two stages and requires rotating the table 180° to provide the surgeon access to the contralateral chest for the second stage of the operation. The anesthesiologist must be cautious during these changes to avoid problems with the airway and to ensure that the lines and monitor wires have enough slack to accommodate changes in position. The anesthesiologist must be aware during these cases about possible injury to the contralateral pleura, especially if CO_2 capnothorax is being used, as the elevated intrathoracic pressure in the contralateral hemithorax can make ventilation difficult and cause cardiovascular collapse or tension pneumothorax because of malfunction of the chest tube. Special attention must be given to the patient's elevated arm and head to prevent crushing injuries with the robotic arms. A recent case report [12] showed a brachial plexus injury in an 18-year-old male after robot-assisted thoracoscopic thymectomy. In this report, the left upper limb was in slight hyperabduction. It is important to keep in mind that hyperabduction of the elevated arm to give optimal space to the operating arm of the robot can lead to a neurologic injury. Close communication between surgeon and anesthesiologist in relation to the positioning and function of the robot is mandatory, and all proper measures must be taken, including the use of soft padding and measures to avoid hyperabduction of the arm. The elevated arm should be protected by using a sling resting device. Operating room staff should always be vigilant of telescope light sources because direct contact of these devices with surgical drapes and the patient's skin can quickly cause serious burns while telescopes and cameras are being changed.

An early report by Bodner et al. [13] involving 13 patients with mediastinal masses resected with the da Vinci® robotic surgical system showed no intraoperative complications or surgical mortality. In this series of patients, a complete thymectomy with en bloc removal of all mediastinal fat around the tumor was performed. In this report, cases were restricted to patients with a tumor size less than 10 cm in diameter.

In a report by Savitt et al. [4] involving 14 patients undergoing robot-assisted thymectomy, all patients received a DLT for selective lung ventilation; in addition, patients were managed with arterial and central venous pressure catheters. Complete thymectomy was performed on all 14 patients. Right-lung deflation was accomplished with selective lung ventilation and CO_2 insufflation to a pressure of 10–15 mmHg to maintain the lung away from the operative area. It is important that the anesthesiologist recognize the effects of CO_2 insufflation in the thoracic cavity. The outcome of this report included no conversion to open thoracotomy, nor any intraoperative complications or deaths; the median hospital stay was 2 days with a range of 1–4 days.

In another report, Rückert et al. [9] had zero mortality and an overall postoperative morbidity rate of 2% in 106 consecutive robot-assisted thymectomies. Therefore, robotic thymectomy is a promising technique for minimally invasive surgery.



FIG. 31.4. Mediastinal mass resection.

Length of stay was shorter with robotic thymectomy when compared to the conventional approach via sternotomy. Figure 31.4 displays a case of mediastinal mass resection.

Robotic-Assisted Pulmonary Lobectomy

With the introduction of the da Vinci® robotic surgical system, there has been widespread interest in its use in minimally invasive surgery involving the chest. A report by Park et al. [14] showed robot-assisted thoracic surgical lobectomy to be feasible and safe. In the report, the operation was accomplished with the robotic system in 30 out of 34 scheduled patients. The remaining four patients required conversion to open thoracotomy. Anderson et al. [15] reported a series of 21 patients that underwent robotic lung resection for lung cancer. In this report, the 30-day mortality and conversion rate was 0%. The median operating room time and blood loss was 3.6 h and 100 mL. The complication rate was 27% and included atrial fibrillation and pneumonia. Gharagozloo et al. [16] reported a series of 100 consecutive robotic-assisted lobectomies for lung cancer and concluded that robotic surgery is feasible for mediastinal, hilar, and pulmonary vascular dissection during video-assisted thoracoscopy lobectomy.

Positioning the patient for a robotic lobectomy includes placing the patient over a bean bag in a maximally flexed lateral decubitus position with the elevated arm slightly extended so that the thoracic cavity can be accessed and no damage to the arm occurs during manipulation of the robotic arms. Patients undergoing robotic lobectomy must have a lung isolation device to achieve OLV. In the vast majority of these cases, a left-sided DLT is used and optimal position is achieved with the flexible fiberoptic bronchoscope [17]. In a few cases in which the airway is deemed to be difficult, an independent bronchial blocker could be used and optimal position achieved with the use of a fiberoptic bronchoscope [18]. Initial thoracic exploration is performed with conventional thoracoscopy to

verify tumor location. During robot-assisted lobectomy, it is mandatory that lung collapse is achieved effectively to allow the surgeon the best field of vision and to avoid unnecessary damage to vessels or lung parenchyma.

All patients undergoing robot-assisted thoracic lobectomy should have an arterial line. The anesthesiologist must be ready for potential conversion to an open thoracotomy. In the Park report [14], three out of four cases that needed to be converted had minor bleeding; in addition, in one case lung isolation was lost, requiring an open thoracotomy. It is mandatory that the anesthesiologist involved in these cases have experience in placing a DLT [19] and can guarantee optimal position with the aid of flexible fiberoptic bronchoscope. Using intraoperative fiberoptic bronchoscopy to make adjustments to the DLT during surgery is challenging because the table is rotated 180° away from the anesthesiologist's field. The chassis of the robot is often positioned over the patients head leaving a very small area for the anesthesiologist to access the airway.

A recent report by Gharagozloo et al. [16] involving 100 patients who underwent lobectomy and complete mediastinal nodal dissection for early stage lung cancer (stage I and II) with the robotic system reported one nonemergent conversion to open thoracotomy. In this report, postoperative analgesia was managed with the infusion of a local anesthetic (0.5% bupivacaine, 4 mL/h) through catheters placed in a subpleural tunnel encompassing intercostal spaces 2 through 8. All patients were extubated in the operating room. Mean operating room time was 216 min (range 173–369). Overall mortality within 30 days was 4.9%, and median length of stay was 4 days. Postoperative complications included atrial fibrillation in four cases, prolonged air leak in two cases, and pleural effusion requiring drainage in two cases – complications that are not different from those occurring with video thoracoscopic surgery. Although lobectomy can be performed via robot-assisted surgery, the advantages at present are not well defined. In contrast, the increasing surgical times, the increased number of operating room personnel needed, and the cost and outcomes of robotic surgery need to be studied and compared with thoracoscopic lobectomy.

Carbon Dioxide Insufflation During Robotic Surgery

Continuous low-flow insufflation of CO₂ has been demonstrated as an aid for surgical exposure during minimally invasive thoracic procedures. It has been used as the only means of providing surgical exposure to the thoracic cavity (during two-lung ventilation for VATS), or more frequently in conjunction with a DLT or an independent bronchial blocker and OLV. The compression of the lung parenchyma by CO₂ acts as a retractor [20].

A study by Ohtsuka et al. [21] involving 38 patients undergoing minimally invasive internal mammary harvest during cardiac surgery found significant increases in mean central

venous pressure, pulmonary artery pressure, and the pulmonary artery wedge pressure. They also found that with insufflation of the right hemithorax, but not the left side, slight decreases were noted in the mean arterial blood pressure and cardiac index. They concluded that the hemodynamic effect from continuous insufflation of CO_2 at 8–10 mmHg for 30–40 min is mild in both hemithoraces, although the impact is greater on the right. This information was supported by another study [22]. This study involving 20 patients undergoing thoracoscopic sympathectomy and concluded that compared to the left side hemithorax the impact of CO_2 insufflation on the vena cava and the right atrium during right-sided procedures was associated with reduction of venous return and low cardiac index and stroke volume. The impact of CO_2 insufflation on the respiratory system has also been studied. El-Dawlatly et al. [23] reported a significant pressure-dependent increase in peak airway pressure and a decrease in dynamic lung compliance but no difference in tidal volume or minute ventilation during volume-controlled ventilation.

Insufflation of CO_2 should only be started after initial thoracoscopic evaluation has ruled out that the port of insufflation has not compromised a vascular structure or the lung parenchyma. Communication between the surgeon, anesthesiologist, and operating room personnel is crucial at this point. Insufflation is ideally started at low pressures of 4–5 mmHg and is gradually increased while monitoring the patient's vital signs. The anesthesiologist should always be aware of the possibility of gas embolization during these cases. In the case of sudden cardiac collapse, the CO_2 flow should be discontinued immediately. Ventilation during CO_2 insufflation should be titrated to keep adequate oxygenation and a normal PaCO_2 and pH. Also, damage to the contralateral pleura may occur resulting in CO_2 flow to the contralateral chest, making ventilation difficult and also causing hemodynamic compromise, along with the potential development of subcutaneous emphysema.

Robotic-Assisted Esophageal Surgery and Anesthetic Implications

Transthoracic esophagectomy with extended lymph node dissection is associated with higher morbidity rates than transhiatal esophagectomy. Esophagectomy is a palliative and potentially curative treatment for esophageal cancer. Minimally invasive esophagectomy has been performed to lessen the biological impact of surgery and potentially reduce pain. The initial esophagectomy experience with the da Vinci® robot surgical system involved a patient who had a thoracic esophagectomy with wide celiac axis lymphadenectomy. The case was reported by Kernstine et al. [24] and had promising results. Thereafter another report using the da Vinci® robot surgical system has been published of 6 patients undergoing esophagectomy without intraoperative complications [25]. The surgical approach in this report was performed from the right side of the chest. A left-sided DLT was used

to selectively collapse the right lung while, at the same time, ventilation was maintained in the left lung.

In a report by Hillegersberg et al. [26] involving 21 consecutive patients with esophageal cancer who underwent robot-assisted thoracoscopic esophagolymphadenectomy, 18 were completed thoracoscopically and 3 required open procedures (because adhesions or intraoperative hemorrhage). In this case series report, all patients received a left-sided DLT and a thoracic epidural catheter as part of their anesthetic management. Positioning of these patients was in a left lateral decubitus position, and the patient was tilted 45° towards the prone position. Once the robotic thoracoscopic phase was completed, the patient was then put in supine position and a midline laparotomy was performed. A cervical esophagogastrostomy was performed in the neck for the completion of surgery.

Of interest in this series is the fact that pulmonary complications occurred in the first 10 cases (60%), caused primarily by left-sided pneumonia and associated acute respiratory distress syndrome in 3 patients (33%). These complications were probably related to barotrauma to the left lung (ventilated lung) attributed to high tidal volumes and high peak inspiratory pressures. In the 11 patients that followed, the same authors modified their ventilatory setting to administer continuous positive airway pressure ventilation 5 cm H_2O during single-lung ventilation and pressure-controlled ventilation was used; with this approach the respiratory complication rate was reduced to 32%.

A recent report by Kim et al. [27] described 21 patients who underwent robotic-assisted thoracoscopic esophagectomy performed in a prone position with the use of a Univent® bronchial blocker tube (Fuji Systems Corp, Tokyo Japan). All thoracoscopic procedures were completed with robotic-assisted techniques followed by a cervical esophagogastrostomy. In Kim's report, major complications included anastomotic leakage in 4 patients, vocal cord paralysis in 6 patients, and intraabdominal bleeding in 1 patient. The prone position led to an increase in central venous pressure and mean pulmonary arterial pressure and a decrease in static lung compliance. The overall conclusion from this report is that robotic assistance esophagectomy in the prone position is technically feasible and safe. Others have reported a robotic-assisted transhiatal esophagectomy technique feasible and safe as well [28].

Another study [5] involved 14 patients who underwent esophagectomy using the da Vinci® robot surgical system in different surgical stages. It showed that for a complete robotic esophagectomy including laparoscopic gastric conduit, the operating room time was an average of 11 h with a console time by the surgeon of 5 h, and an estimated mean blood loss of 400 ± 300 mL. In this report after the robotic thoracoscopic part of the surgery was accomplished with the patient in the lateral decubitus position, patients were then placed in supine position and reintubated, and the DLT was replaced with a single-lumen endotracheal tube. The head of each patient was turned upward and to the right, exposing the left neck for the cervical part of the operation. Among the pulmonary

TABLE 31.3. Complications of robotic-assisted thoracic surgery.

References	n=cases	Operation	Intraoperative complications	Postoperative complications
Rea et al. [3]	33	Thymectomy	0	Chylothorax n=1 Hemothorax n=1
Savitt et al. [4]	15	Mediastinal mass resection	0	Atrial fibrillation n=1
Kernstine et al. [5]	14	Esophagectomy	Conversion to open procedure n=1	Thoracic duct leak n=3 Vocal cord paralysis n=3 Atrial fibrillation n=5
Rückert et al. [9]	106	Thymectomy	Bleeding n=1	Phrenic nerve injury n=1
Pandey et al. [12]	1	Thymectomy	—	Brachial plexus injury
Bodner et al. [13]	14	Mediastinal mass resection	0	Postoperative hoarseness due to lesion to left laryngeal recurrent nerve
Park et al. [14]	34	Lobectomy	Conversion to open thoracotomy n=3 Lack lung isolation n=1	Supraventricular arrhythmia n=6 Bleeding n=1 Air leak n=1
Gharagozloo et al. [16]	100	Lobectomy	0	Atrial fibrillation n=4 Air leak n=2 Bleeding n=1 Pleural effusion n=2
Van Hillegersberg et al. [26]	21	Esophagectomy	Conversion to open procedure n=3	Pulmonary complication 60% first 10 cases Pulmonary complication 32%, 11 patients
Kim et al. [27]	21	Esophagectomy	Bleeding n=1	Anastomotic leakage n=4 Vocal cord paralysis n=6

complications in the postoperative period, arterial fibrillation occurred in 5 out of 14 patients.

In Kernstine's report [5] among the recommendations to improve efficiency in these cases is the "use of an experienced anesthesiologist who can efficiently intubate and manage single-lung ventilation and hemodynamically support the patient during the procedure." This follows what Nifong and Chitwood [19] have reported in their editorial views regarding anesthesia and robotics: that a team approach with expertise in these procedures involving nurses, anesthesiologists, and surgeons with an interest in robotic procedures is required.

The data on robotic-assisted esophagectomy suggest that the procedure is safe, feasible, and associated with preoperative outcomes similar to open and minimally invasive esophagectomy. No data, however, demonstrate improved outcomes in terms of operative morbidity, pain, operative time, or total costs [29]. Table 31.3 displays the complications of robotic-assisted thoracic surgery involving the mediastinum lung and esophagus.

Summary

The use of the da Vinci® robot surgical system in thoracic and esophageal surgery continues to gain acceptance. Although its use has reduced surgical scarring and decreased length of stay, specific indications for use in these areas need to be determined. All reports to date describe the use of lung isolation devices, most often a left-sided DLT, as part of the intraoperative management of thoracic surgery patients to facilitate surgical exposure. In addition, because the surgical approach varies

depending on the thoracic procedure, optimal positioning is not standard, and varies among the specific surgical procedures. Vigilance is required with patients' elevated arms to avoid nerve injuries or crush injuries from the robotic arms. Continuous low-flow insufflation of CO₂ has been used as an aid for surgical exposure during minimally invasive thoracic procedures. The potential to convert to an open thoracotomy requires preparation by the surgical team and anesthesiologist. The use of the da Vinci® robot surgical system is expected to grow in the years to come [30, 31]. Prospective studies are needed to define the specific advantages of this robotic system.

References

1. Tatooles AJ, Pappas PS, Gordon PJ, Slaughter MS. Minimally invasive mitral valve repair using the da Vinci robotic system. Ann Thorac Surg. 2004;77:1978-82.
2. Nifong LW, Chitwood WR, Pappas PS, Smith CR, Argenziano M, Starnes VA, et al. Robotic mitral valve surgery: a United States multicenter trial. J Thorac Cardiovasc Surg. 2005;129:1395-404.
3. Rea F, Marulli G, Bortolotti L, Feltracco P, Zuin A, Sartori F. Experience with the "da Vinci" robotic system for thymectomy in patients with myasthenia gravis. Ann Thorac Surg. 2006;8:455-9.
4. Savitt MA, Gao G, Furnary AP, Swanson J, Gately HL, Handy JR. Application of robotic-assisted techniques to the surgical evaluation and treatment of the anterior mediastinum. Ann Thorac Surg. 2005;79:450-5.
5. Kernstine KH, DeArmond DT, Shamoun DM, Campos JH. The first series of completely robotic esophagectomies with three-field lymphadenectomy: initial experience. Surg Endosc. 2007;21:2285-92.
6. Mack MJ. Minimally invasive and robotic surgery. JAMA. 2001;285:568-72.

7. Campos JH. An update on robotic thoracic surgery and anesthesia. *Curr Opin Anaesthesiol*. 2010;23:1–6.
8. Bodner J, Wykypiel H, Wetscher G, Schmid T. First experiences with the da Vinci operating robot in thoracic surgery. *Eur J Cardiothorac Surg*. 2004;25:844–51.
9. Rückert JC, Ismail M, Swierzy M, Sobel H, Rogalla P, Meisel A, et al. Thoracoscopic thymectomy with the da Vinci robotic system for myasthenia gravis. *Ann NY Acad Sci*. 2008;1132:329–35.
10. Baraka A. Onset of neuromuscular block in myasthenic patients. *Br J Anaesth*. 1992;69:227–8.
11. Abel M, Eisenkraft JB. Anesthetic implications of myasthenia gravis. *Mt Sinai J Med*. 2002;69:31–7.
12. Pandey R, Elakkumanan LB, Garg R, Jyoti B, Mukund C, Chandralekha, et al. Brachial plexus injury after robotic-assisted thoracoscopic thymectomy. *J Cardiothorac Vasc Anesth* 2009;23:584–6.
13. Bodner J, Wykypiel H, Greiner A, Kirchmayr W, Freund MC, Margreiter R, et al. Early experience with robot-assisted surgery for mediastinal masses. *Ann Thorac Surg*. 2004;78:259–65.
14. Park BJ, Flores RM, Rusch VW. Robotic assistance for video-assisted thoracic surgical lobectomy: technique and initial results. *J Thorac Cardiovasc Surg*. 2006;131:54–9.
15. Anderson CA, Filsoufi F, Aklog L, Farivar RS, Byrne JG, Adams DH. Robotic-assisted lung resection for malignant disease. *Innovations*. 2007;2:254–8.
16. Gharagozloo F, Margolis M, Tempesta B, Strother E, Najam F. Robot-assisted lobectomy for early-stage lung cancer: report of 100 consecutive cases. *Ann Thorac Surg*. 2009;88:380–4.
17. Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic anesthesia. *Curr Opin Anaesthesiol*. 2009;22:4–10.
18. Campos JH. Progress in lung separation. *Thorac Surg Clin*. 2005;15:71–83.
19. Nifong LW, Chitwood Jr WR. Challenges for the anesthesiologist: robotics? *Anesth Analg*. 2003;96:1–2.
20. Wolfer RS, Krasna MJ, Hasnain JU, McLaughlin JS. Hemodynamic effects of carbon dioxide insufflation during thoracoscopy. *Ann Thorac Surg*. 1994;58:404–7.
21. Ohtsuka T, Nakajima J, Kotsuka Y, Takamoto S. Hemodynamic response to intrapleural insufflation with hemipulmonary collapse. *Surg Endosc*. 2001;15:1327–30.
22. El-Dawlatly AA, Al-Dohayan A, Samarkandi A, Algahdam F, Atef A. Right vs left side thoracoscopic sympathectomy: effects of carbon dioxide insufflation on haemodynamics. *Ann Chir Gynaecol*. 2001;90:206–8.
23. El-Dawlatly AA, Al-Dohayan A, Abdel-Meguid ME, Turkistani A, Alotaibi WM, Abdelaziz EM. Variations in dynamic lung compliance during endoscopic thoracic sympathectomy with carbon dioxide insufflation. *Clin Auton Res*. 2003;13 Suppl 1:I94–7.
24. Kernstine KH, DeArmond DT, Karimi M, Van Natta TL, et al. The robotic, 2-stage, 3-field esophagolymphadenectomy. *J Thorac Cardiovasc Surg*. 2004;127:1847–9.
25. Bodner JC, Zitt M, Ott H, Wetscher GJ, et al. Robotic-assisted thoracoscopic surgery (RATS) for benign and malignant esophageal tumors. *Ann Thorac Surg*. 2005;80:1202–6.
26. van Hillegersberg R, Boone J, Draaisma WA, Broeders IA, et al. First experience with robot-assisted thoracoscopic esophagolymphadenectomy for esophageal cancer. *Surg Endosc*. 2006;20:1435–9.
27. Kim DJ, Hyung WJ, Lee CY, Lee JG, Haam SJ, Park IK, et al. Thoracoscopic esophagectomy for esophageal cancer: feasibility and safety of robotic assistance in the prone position. *J Thorac Cardiovasc Surg*. 2010;139:53–9.
28. Gutt CN, Binttan VV, Köninger J, Müller-Stich BP, Reiter M, Büchler MW. Robotic-assisted transhiatal esophagectomy. *Langenbecks Arch Surg*. 2006;391:428–34.
29. Watson TJ. Robotic esophagectomy: is it an advance and what is the future? *Ann Thorac Surg*. 2008;85:757–9.
30. Czibik G, D'Ancona G, Donias HW, Karamanoukian HL. Robotic cardiac surgery: present and future applications. *J Cardiothorac Vasc Anesth*. 2002;16:495–501.
31. Hubens G, Ruppert M, Balliu L, Vaneerdeweg W. What have we learnt after two years working with the da Vinci robot system in digestive surgery? *Acta Chir Belg*. 2004;104:609–14.

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Key Points

- From a physiologic point of view the alveolar–capillary membrane is the most important part of respiratory system. It always undergoes micro-injury during cardiac surgery with the use of cardiopulmonary bypass (CPB). Therefore, a second insult, such as loss of part of the pulmonary parenchyma, can lead to acute lung injury and unfavorable outcomes from combined thoracic and cardiac procedures.
- Additional insult to respiratory system can be caused by phrenic nerve injury and subsequent diaphragmatic dysfunction and disturbances in chest wall mechanics caused by sternotomy.
- Clinicians should be very selective in choosing to combine pulmonary resection and heart surgery. Concomitant pulmonary resection and cardiac surgery entail substantial additional risk, especially pulmonary complications and bleeding problems.
- Anesthetic management must be individualized and based on preoperative assessment, extent of surgery, and need to use CPB. Anesthesiologists managing these cases should have extensive training in both cardiac and thoracic anesthesia. An expertise in transesophageal echocardiography is also desired.

Introduction

Combined cardiac and thoracic procedures are rare. Anesthesia and optimal perioperative management for these complex, high-risk surgical interventions requires an expertise in both cardiac and pulmonary physiology, lung isolation techniques, the multiorgan impact of cardiopulmonary bypass (CPB), and additional monitoring techniques (e.g., transesophageal echocardiography, TEE). Combined procedures may include excision of invasive tumors, pulmonary endarterectomy, cardiac revascularization combined with lung resection, and cardiac procedures combined with lung transplantation (e.g., PFO closure). Optimal management of these procedures remains controversial and is not well described [1]. Proponents of single-stage operations will argue in favor of the avoidance of a second surgery and anesthetic and reduced hospital stay [1, 2]. The opponents will argue for divided, two-stage procedures on the basis of limiting surgical trauma, blood loss, multiorgan impact of CPB, high intensive care morbidity, and thus may potentially confer a better long-term survival [2, 3].

The following chapter will briefly describe the anesthetic management for various combined thoracic and cardiac procedures. For a better understanding of why CPB is detrimental for lung function the author will briefly describe the structure

and function of the air–blood barrier and the pathophysiology of its injury during procedures with use of CPB.

Structure of the Alveolar–Capillary Barrier

The human lung consists of 30,000,000 alveoli. Each of them has a dense network of capillaries, which form air–blood barriers (alveolar–capillary membranes). From a physiological point of view, the air–blood barrier is the most important part of the respiratory system. It is the site of gas exchange. Additionally, the alveolar–capillary barrier separates the external environment from the pulmonary circulation, regulates transport of fluid and molecules from alveoli to capillaries, and is a vital part of the natural defense mechanism of the human body (see also Chap. 7) [4].

Structure

The alveolar–capillary barrier has three components: thin processes of type I pneumocytes (epithelial cells), endothelial cells, and their common basement membranes (Fig. 32.1). Typically, endothelial and epithelial cells have separate basement membranes, but the pulmonary alveolus is a unique site where the basement membranes are fused together. This creates an extremely thin barrier (0.2–0.4 μm) enabling efficient exchange of oxygen and carbon dioxide [5, 6]. The processes of type I pneumocytes are very thin and cover 95% of the alveolar surface. The remaining 5% is covered by type II pneumocytes, which produce surfactant. Type II pneumocytes (also called granular cells) reside within the corners of

the alveoli because their large cellular structure makes them inefficient for gas exchange (Fig. 32.1). Type II pneumocytes eventually divide into type I pneumocytes (progenitor cells). During injury of the alveolar surface, the damaged type I pneumocytes are replaced by large, cubical, quickly dividing, type II pneumocytes. These large cuboidal cells create a thicker alveolar–capillary barrier leading to inefficient gas exchange.

Tight intercellular junctions between epithelial cells (pneumocytes) are impermeable to fluid, which contrasts with endothelial cell junctions which are highly permeable to fluids and allow the continuous exchange of plasma components between capillaries and the pulmonary interstitium. The common basement membrane consists of laminin, glycosaminoglycans, collagen type IV, and fibronectin [5–7]. Glycosaminoglycans are concentrated on one side of basement membrane regulating its permeability. Among all the components of the alveolar–capillary barrier this is the most critical part and its injury leads to permanent damage of the blood–gas interface [8, 9]. There are three stabilizing elements of the alveolar–capillary barrier: surfactant, the pulmonary circulation, and the connective tissue of the intra-alveolar septa [6, 10].

Surfactant

Surfactant is composed from lipids (90%) and proteins (10%). The lipid component mainly consists of phosphatidylcholine (bipolar lipid) and phosphatidylglycerol [11]. Both lipids have a hydrophilic “head” and “lipophilic” tail (see Fig. 32.1a, right-hand inset). Surfactant forms a monolayer lining the alveolar surface with the hydrophilic part directed towards the

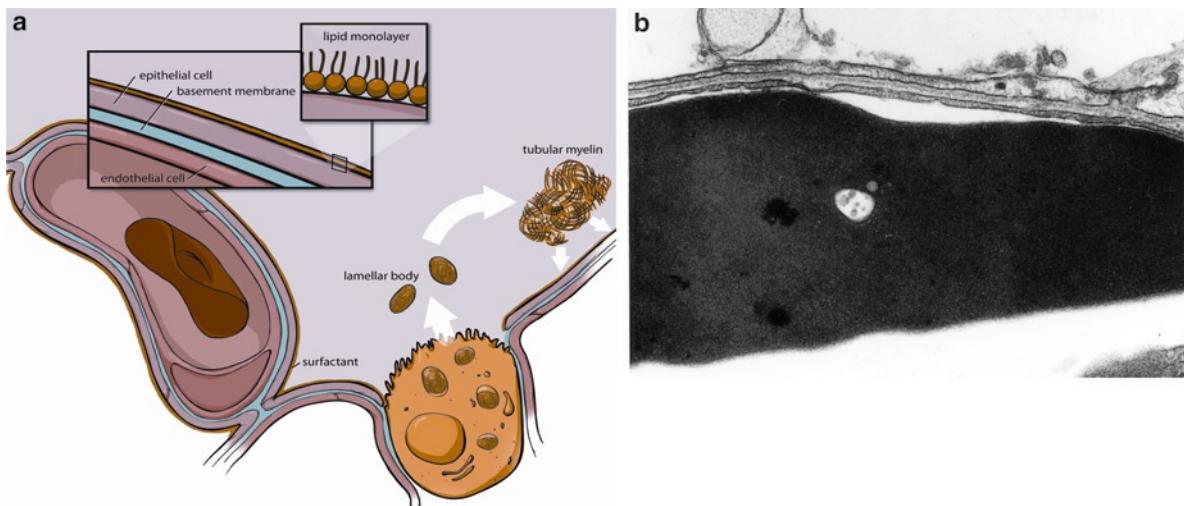


FIG. 32.1. (a) The picture presents a scheme of an air–blood barrier, which consist of endothelial cell, epithelial cell (type I pneumocyte), and their common basement membrane. The large cuboidal cell is type II pneumocyte producing surfactant contained within its cytoplasm as lamellar bodies (onion-like structures), which are exocytosed into the alveolar lumen, then transformed into tubular myelin, and finally monolayered on the surfactant covering the surface of type I pneumocytes. The left-hand side inset shows details of the thin alveolar–capillary membrane and the right-hand side inset shows a scheme of the surfactant monolayer. (b) Electron microscope photograph which is showing an air–blood barrier.

epithelial cells. The biochemical structure of the pulmonary surfactant resembles a detergent, surface-active layer, which aims to lower the surface tension and stabilizes the alveolar shape and structure. Surfactant protects the alveolus from collapse and prevents overdistension [12]. Moreover, surfactant acts as an antipulmonary edema substance.

The protein component consists of four, distinct surfactant proteins – A, B, C, and D (SP-A surfactant protein A, SP-B, SP-C, and SP-D). These molecules play an important role in local defense mechanisms, surfactant metabolism, recirculation, and spreading on the alveolar surface. Additionally, they participate in local defense mechanisms. SP-A is a 28,000–36,000 kD protein and participates in monolayer formation and in recirculation of pulmonary surfactant. It has hydrophilic character. SP-D is the biggest surfactant protein (42,000 kD), has also hydrophilic character and its main role is to regulate local defense mechanisms. SP-B and -C are relatively small proteins (9,000 and 4,000 kD, respectively) with lipophilic character, they are essential for monolayer formation [13]. Surfactant is produced in type II pneumocytes and is seen as so-called lamellar bodies (onion like structures) (Fig. 32.2). Lamellar bodies are excreted into the alveolar lumen, transform into tubular myelin (Fig. 32.3), and then spread as a monolayer on the surface of type I pneumocytes (Fig. 32.1). The metabolism of surfactant is unique, it is recycled. Molecules of surface-active material are endocytosed back into type II pneumocytes and without any breakdown incorporated back into the lamellar bodies. Small amounts of surfactant

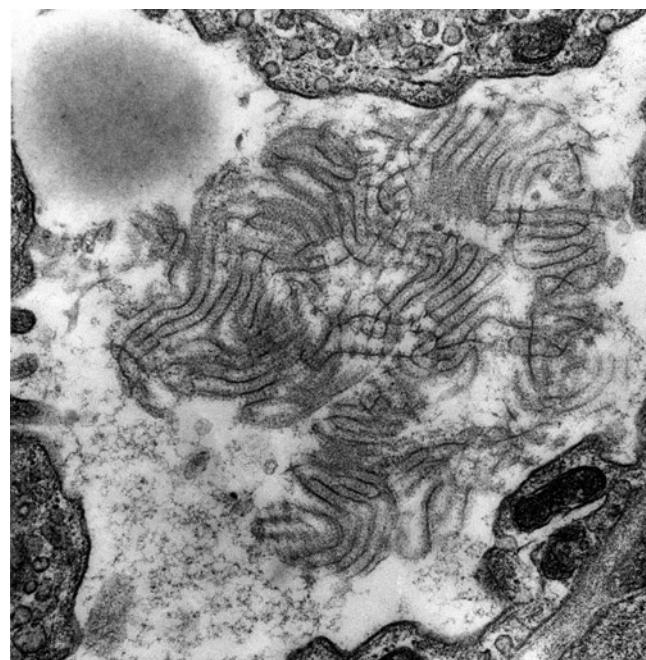


FIG. 32.3. Electron microscope picture, which presents structure of the tubular myelin.

(7–8%) are digested by alveolar macrophages. In the normal physiological situation, surfactant is not present within the pulmonary circulation (except for newborns when the lung is drying out after delivery). If surfactant is present within the pulmonary circulation, its amount reflects the extent of damage to the alveolar–capillary barrier [14, 15].

Pulmonary Circulation

Flow through the pulmonary circulation equals systemic flow enabling effective gas exchange. The pulmonary circulation also plays an important role in the metabolic and filtrating functions of the lung. The pulmonary circulation is a low-pressure system, which is influenced by gravitation forces creating West's zones. The alveolar capillaries make contact with multiple alveoli, which increases the efficiency of gas exchange. The alveolar vessels are stabilized by a delicate network of collagen and elastic fibers, which form a continuum connected to basement membranes of the air–blood barriers. The location and structure of the alveolar capillaries make them susceptible to pressure changes occurring within the alveolar space. Rising intra-alveolar pressure will decrease the volume of the alveolar capillaries and increase their resistance.



FIG. 32.2. Electron microscope photograph showing a type II pneumocyte filled with lamellar bodies (onion-like structures), some of them exocytosed into the lumen of the alveolar space.

Connective Tissue

The connective tissue (mesenchyma) of the inter-alveolar septae is responsible for both their elasticity and mechanical resistance [10, 16]. The mesenchyma consists of cellular and extracellular components. The cellular part is largely composed from fibroblasts, which are responsible for

producing extracellular elements of the connective tissue, for example, collagen fibers, elastic fibers, fibronectin, entactin, glycosaminoglycans, and components of the basement membranes [6]. The extracellular connective tissue forms a continuum extending from the hilum into each alveolus [17]. Thus, any structural change within the lung tissue will have a transmitted effect upon every alveolus. This means that any change of shape within the lung affects every alveolus. Collagen fibers form the main mechanical support and restrictive force. This is counterbalanced by the presence of elastic fibers, which are responsible for the elastic recoil of lung parenchyma and its compliance. Collagen fibers are interwoven with elastic fibers and both elements aid in stabilization of the alveolar–capillary membranes. During injury, the elastic fibers are more susceptible to damage, which creates an imbalance in the resistive–elastic forces of the lung in favor of a stiffer lung with low compliance.

Lung Injury During Surgery with Use of Cardiopulmonary Bypass

Combined cardiac and thoracic surgical procedures with the use of CPB are controversial. If a cardiac procedure is performed with the use of CPB and is combined with thoracic surgery, which involves resection of lung parenchyma (lobectomy or pneumonectomy), respiratory complications may reach an incidence as high as 49% [18, 19]. It is postulated that CPB is the main causative factor of the aforementioned complications; therefore, the most common injuries of respiratory system caused by CPB will be briefly described in the following paragraphs [20–22].

Respiratory complications occurring after cardiac surgery with use of CPB are relatively common but the vast majority are mild and self-limiting [23, 24]. It is important to emphasize that the cause of lung failure after operations involving CPB is multifactorial [25, 26]; patient factors combine with the direct detrimental effects of CPB to compromise pulmonary function in the early postoperative period. A second insult to the respiratory system, such as loss of part of the pulmonary parenchyma, can be detrimental and lead to acute lung injury (ALI) and unfavorable outcomes.

The most severe forms, acute respiratory distress syndrome (ARDS) or ALI, occur in 1–2% of cardiac cases with a very high mortality (40%) [9, 23].

Histological Injury

Most patients who undergo cardiac surgery with the use of CPB present some degree of histological lung injury [27]. Microscopic observations reveal a range of injuries detected within the structures of the air–blood barriers [8, 27, 28]. Mild injury presents as edema of endothelial (type I pneumocytes) and epithelial cells. More severe forms cause denuding of the

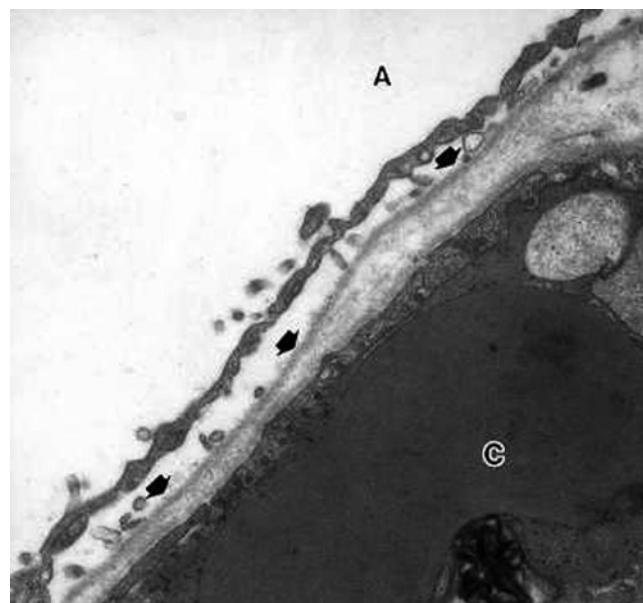


FIG. 32.4. Electron microscope photograph presenting a portion of alveolar–capillary barrier with partially “denuded” basement membrane (arrows). A—alveolar lumen, C—capillary lumen. Permission for publication obtained from Taylor & Francis (Reprinted with permission from Wąsowicz M, Sobczyński P, Drwiła R, Biczysko W, Marszałek A, Andres J. Air–blood barrier injury during cardiac operations with the use of cardiopulmonary bypass (CPB). An old story? *Scand Cardiovasc J* 2003; 37: 216–221).

basement membranes with loss of epithelial lining (Fig. 32.4). In the most severe cases, basement membranes of alveolar–capillary membranes lose their continuity, which means they are permanently damaged. The alveoli with damaged basement membrane fill with fluid and lamellar bodies (surfactant) are not able to spread on the surface of epithelial cells. Beyond the damage visualized within the alveolar–capillary membranes, authors have observed congestion within alveolar capillaries, and the accumulation of polynuclear leukocytes (neutrophils), many of which are extravasated (Fig. 32.5). Upon migrating from the intravascular space into the interstitium or alveolar space, neutrophils are able to survive for 6 h. Subsequent breakdown of neutrophils will exacerbate alveolar damage by releasing an abundance of proteolytic enzymes, reactive oxygen species, and free radicals [29, 30]. In summary, in all patients undergoing surgery utilizing CPB some injury will occur within the pulmonary parenchyma [8, 27, 28].

Systemic Inflammatory Response Syndrome

CPB causes a systemic inflammatory response syndrome (SIRS) [29–33]. This leads to the activation of neutrophils, macrophages, and multiple cytokines including complement, and is commonly associated with free radical

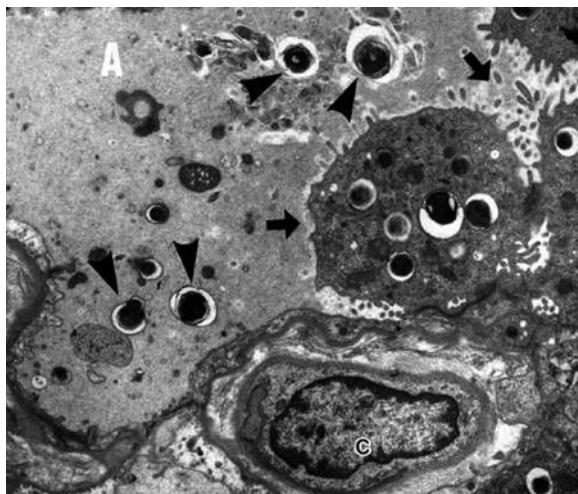


FIG. 32.5. Electron microscope photograph showing severe microscopic injury of an air–blood barrier occurring post-CPB. The alveolar lumen is filled with edema fluid and surfactant structures (lamellar bodies–arrow heads) are not able to spread. The arrows indicate type II pneumocytes. Permission for publication obtained from Taylor & Francis (Reprinted with permission from Wąsowicz M, Sobczyński P, Drwiła R, Biczysko W, Marszałek A, Andres J. Air–blood barrier injury during cardiac operations with the use of CPB. An old story? *Scand Cardiovasc J* 2003; 37: 216–221).

formation [30–35]. Complement proteins, mainly C3a and C5a, promote neutrophil activation, which can subsequently adhere to the endothelial cells and migrate into the interstitium promoting local damage and inflammation [34, 35]. The lung acts as a “filter” to activated neutrophils and therefore is often more vulnerable to CPB-related injury compared to other organs [4]. In addition to the release of proinflammatory mediators and enzymes, activated neutrophils express surface receptors, CD11a and CD 18b, which facilitate further leukocyte–endothelial adhesion and chemotaxis. Those activated neutrophils, which remain within the lumen of the alveolar capillaries tend to accumulate in congested blood vessels and release their contents causing “leakage” from alveolar capillaries into the extracellular spaces and alveolar lumen [27–29]. Neutrophils are not the only cells, which are activated by an extracorporeal circuit. Macrophages also belong to the first line of cells, which are stimulated by CPB [35]. They release multiple cytokines. The main cytokines involved in the inflammatory process and lung injury are interleukin 6 and 8. At the end of CPB their concentration within the alveolar lining is much higher than within plasma [30, 31, 33].

Lipid Peroxidation

Another line of activation caused by CPB is lipid peroxidation and release of free radicals [36]. They are mainly freed as a consequence of ischemia–reperfusion injury. It should be stressed that during aortic cross-clamp the lung has no blood

supply, except for a small amount of flow coming from the bronchial arteries. During reperfusion large amounts of free radicals are flushed from ischemic lung tissue (as a result of xanthine oxidase activation) [15]. Free radicals have a high affinity for cellular membranes causing oxidation of lipid components (so-called peroxidation) [37]. Free radicals also activate leukocytes [23].

Surgical Factors

CPB is not the only cause of respiratory system dysfunction after cardiac surgery. Other common factors include:

- Changes in lung mechanics related to sternotomy, internal mammary artery harvesting, and other surgical manipulations. This presents as an increased elastance of the pulmonary tissue (decreased compliance). Decreased compliance is also caused by the injury caused by CPB, i.e., increased pulmonary vasculature permeability, positive fluid balance, and accumulation of neutrophils [38].
- Atelectasis is a common postoperative complication after any major, prolonged surgery performed under general anesthesia. Atelectasis occurs in up to 70% of patients undergoing cardiac surgery with or without the use of CPB [25, 38]. After cardiac surgery, atelectasis is observed most frequently in the left lower lobe and is considered the most common cause of an increased alveolar–arterial PO_2 gradient [39]. Atelectasis is also thought to be one of the main factors leading to further inflammatory injury leading to further deterioration in pulmonary function during the recovery phase after cardiac surgery. During the postoperative period, atelectasis is aggravated by pleural effusion (s) or pneumothorax, which may develop as a result of mechanical ventilation, central line cannulation, or air leaks from surgical manipulations [9, 23, 25].
- Phrenic nerve injury leading to poor diaphragmatic function. The most common cause of phrenic nerve injury is the use of cold saline flush or ice slush as a method of additional cardiac preservation. Fortunately, most centers have abandoned this method of cardioprotection.
- Postoperative infections – pneumonia. All the aforementioned factors impairing pulmonary mechanics and ciliary clearance increase the risk of postoperative infections. Moreover, if a patient remains intubated for a prolonged period of time after any cardiac procedure the risk of ventilator associated pneumonia (VAP) increases to 44% (after 7 days of intubation) [40]. Other significant risk factors for postoperative pulmonary infectious complications include cigarette smoking (a very common habit in patients undergoing combined cardiac and thoracic surgery) and the use of H_2 blockers [41].
- Massive transfusions of red blood cells and other blood products also contribute to respiratory dysfunction postoperatively [42, 43].

Prevention of Lung Injury After Cardiac Procedures

Although severe lung injury after CPB (ARDS) is uncommon (1–2%), other pulmonary complications remain a significant cause of mortality and morbidity after cardiac surgery [9, 24]. There are many patient-related risk factors, which contribute to postoperative pulmonary dysfunction, some of them are modifiable. Among most important ones are smoking, obesity, COPD (see Chap. 2), and use of proton pump inhibitors [38, 41].

There is little doubt that CPB is considered a “main culprit” of the pulmonary dysfunction occurring after cardiac surgery, however other factors also play an important role in their pathogenesis. Since the pathophysiology of respiratory complications following cardiac surgery has been extensively studied for last 40 years, clinicians have developed multiple strategies to prevent them [23]. One of the most common approaches is the avoidance of CPB, which can be applied to coronary artery bypass surgeries [43]. On the other hand, currently available results are still inconclusive as to the true benefits of the “off-pump” (OP) CABG. Certainly, the new types of oxygenators (hollow fiber) and use of centrifugal pumps instead of roller pumps decrease activation of neutrophils and subsequent pulmonary dysfunction. The addition of leuko-reduction filters which filter out activated polynuclear leukocytes has also been proven to have a beneficial effect [24, 25]. Similarly, a beneficial effect is observed with the use of heparin-coated circuits. Alternatively, some authors propose the use of the patient’s lungs as a natural oxygenator (so-called Drew-Anderson technique) [44]. Even though it improves the function of the respiratory system after surgery it increases the complexity of the surgical technique (additional cannulation sites) and makes it impractical for combined cardiothoracic procedures. It seems that a much easier approach would be to continue ventilation with small tidal volumes, PEEP, and the use of air during the surgical procedure and use of the vital capacity maneuver just prior discontinuation of CPB [45]. One of the oldest methods used in the cardiac surgery aiming to attenuate of detrimental effects of CPB (including pulmonary dysfunction) is use of corticosteroids [46]. Even though use of methylprednisolone decreased the release of inflammatory interleukins (IL-6 and -8) and complement activation, it has been frequently proven to work as a double-edge sword. While preventing pulmonary complications it can contribute to other significant postoperative problems (sternal wound infection, insulin resistance, and abdominal complications).

Among the many methods aimed at prevention of respiratory complications we should also mention strategies used during the postoperative period. They include use of low-tidal volume ventilation, active preventions of VAP (detailed discussion is beyond the scope of this chapter), early extubation whenever possible and aggressive physiotherapy and incentive spirometry. One of the keys to achieve the above mentioned aims

is to maintain effective pain control during the postoperative period.

In summary, the incidence of postoperative pulmonary complications occurring after cardiac surgery is high. Progress in their prevention and advance in surgical and anesthetic techniques makes most of them temporary. On the other hand, given that many patients currently undergoing cardiac surgery are older and suffering from many comorbidities this is probably the main reason for reluctance to perform combined cardiac and thoracic procedures. The main argument against combined procedures is that most of the patients suffer some degree of lung injury related to the use of CPB and an additional insult to lung tissue caused by surgical resection might significantly increase mortality and morbidity [47, 48].

Surgical Considerations

Many thoracic surgeons are familiar with techniques of extracorporeal circulation. There are some thoracic procedures, which are routinely performed with use of CPB. Among the most common are lung transplantation and pulmonary endarterectomy. Since anesthetic management during these procedures is discussed in different chapters of this textbook they will not be further reviewed here (see Chaps. 37 and 38). The scope of the discussion in this section will concentrate on the perioperative management of patients with intrathoracic malignancies invading cardiac or major vascular structures and patients undergoing thoracic surgery who are suffering from coexisting coronary artery disease. Many surgeons are reluctant to perform one stage cardiac–thoracic operation because of the concerns mentioned earlier [47–49]. Additionally, there is anxiety regarding heparin use and the possibility of excessive bleeding. Apart from the injury to pulmonary function, a frightening consideration is the possibility of dissemination of pulmonary malignancy through the use of CPB [18, 49–51]. On the other hand, a one-stage combined procedure avoids the need for a second major thoracic surgery [2, 50, 51]. In the case of coexisting pulmonary malignancy and coronary artery disease, the answer seems to be straightforward [20, 47, 51, 52]. Preoperative revascularizations performed by interventional cardiologists (PCI – primary coronary intervention) may cause significant time delays for subsequent cancer surgery [53]. Thus, combined surgical coronary revascularization and resection of the lung cancer may be the optimal management. In most cases, revascularization can be performed without use of CPB (i.e., OPCABG), therefore the detrimental effects of CPB can be avoided [20, 47, 51]. The results of combined thoracic–cardiac surgeries are encouraging, however published results usually involve small number of patients [19, 20, 54–56].

When considering proper management of thoracic malignancies invading heart structures, it should be mentioned that surgical resection remains the only curative option for most intrathoracic malignancies [49, 50, 57, 58]. Sometimes

conventional thoracic surgical techniques do not allow complete resection of a pulmonary tumor which is invading the heart or large vessels, therefore radical surgical removal may necessitate the use of CPB [49]. The most common examples are tumors involving left atrium or infiltrating the descending portion of the aorta [50, 55].

Most of these procedures are performed via median sternotomy. Surgical exposure to some of the hilar structures is more difficult when compared to a lateral thoracotomy approach. Left lower lobectomy and mediastinal lymph nodes dissection are especially technically challenging when performed via median sternotomy. Probably in most of the cases, mediastinoscopy is indicated initially to rule out mediastinal spread of the disease. All these concerns raise a question as to whether aggressive treatment including surgical resection of lung parenchyma and cardiac or major vascular structures should be a routine management. The answer is clearly no. This mode of treatment should be only performed in departments that are prepared for the complexity of those cases, can offer expertise in both cardiac and thoracic surgery and anesthesia. Moreover, the functional status of the patient prepared for this type of surgery should be excellent to allow them to survive a potential prolonged stay within an intensive care setting.

Anesthetic Management for Combined Cardiac and Thoracic Procedures

The literature describing the anesthetic management of the patient undergoing combined thoracic and cardiac procedures is very scarce and includes mainly case reports [1, 59]. Subsequent paragraphs will try to summarize current information described as individual cases and the experience of the institution where the author practices cardiac and thoracic anesthesia. The anesthesiologist who is looking after the patient who is scheduled to undergo combined thoracic and cardiac surgery should possess an expertise in both cardiac and thoracic anesthesia. Quite often these procedures are complex and require management by two consultants. For most of the cases we also require the presence of perfusionist, who will be either actively involved with management of the case requiring the use of CPB or prepare the machine for extracorporeal circulation in a “stand-by” mode.

Preoperative Assessment

Apart from standard preoperative evaluations before surgery the anesthesiologist preparing the patient for combined cardiac and thoracic procedure must perform a detailed assessment of the respiratory and cardiovascular systems. An extensive description of respiratory system evaluation is described elsewhere (see Chap. 2). Briefly, the anesthesiologist who is assessing the pulmonary function should concentrate on lung mechanics, pulmonary parenchymal function, and

cardio-respiratory reserve. The most popular test performed to assess lung mechanics is spirometry. The value most commonly used by anesthesiologists is the forced expiratory volume in one second (FEV1). FEV1 is also used to calculate the predicted postoperative FEV1 (ppo-FEV1) once part of the pulmonary parenchyma is resected. Values below 30–35% for ppo-FEV1 are considered as predictors of increased risk of respiratory complications and prolonged weaning from mechanical ventilation. Maximal oxygen consumption is used to assess cardiopulmonary reserve and the diffusing capacity of the lung for carbon monoxide is measured to estimate the gas exchange function of lung parenchyma. Any patient being prepared for a combined procedure requires a very careful airway evaluation. Intrathoracic malignancies necessitating these types of procedures often result in airway involvement, causing deviation or invasion of large airways. Moreover, they can infiltrate or compress large vascular structures. Apart from clinical symptoms the anesthesiologist must examine the results of computed tomography (CT) scans, which show precisely the extent of the disease and possible vascular involvement. A preoperative echocardiogram will be complementary to the radiological examination and should be routinely performed before any cardiac surgical procedure.

The “second leg” of preoperative evaluation focuses on the status of the cardiovascular system. The mortality and morbidity of cardiac surgical patients is strongly influenced by their preoperative severity of the illness. The important factors included in most preoperative risk assessment scores include: age, sex, left ventricular function, type of surgery, urgency of the surgery, redo cardiac surgery, unstable angina, congestive heart failure, history of peripheral vascular disease and cerebral vascular disease, renal insufficiency, and history of diabetes. In most cases, this information can be obtained from the medical history, physical examination, and simple laboratory findings including electro- and echocardiogram. Additionally, results of echocardiography provide a detailed description of valve structure and pathology, contractility of the left and right ventricle, and morphology of most the large vessels. In the case of poor ventricular function (ejection fraction <30%), it is recommended to consider an alternative therapeutic approach rather than combined cardiac–thoracic surgery. If the patient suffers from coronary artery disease, the degree of coronary stenosis(es) is assessed preoperatively by cardiac catheterization (coronary angiogram). This information is important for the anesthesiologist who will be intraoperatively assessing the contractility of the particular segments of myocardium with the use of TEE.

Patients who are scheduled to undergo combined cardiac–thoracic surgery frequently suffer from multiple comorbidities. Among the most significant we should mention: peripheral vascular disease, diabetes mellitus, and kidney dysfunction. Most of these comorbidities are aggravated during the perioperative period and this in turn significantly increases mortality and morbidity. The anesthesiologist must collect a detailed list of medications the patient is currently taking.

Anesthetic Management

The anesthesiologist providing care during combined cardiac-thoracic procedures faces multiple challenges. Quite often he/she must simultaneously manage hemodynamic instability, hypoxemia, problems with ventilation, and excessive bleeding. It is beyond the scope of this chapter to fully discuss all of the challenges of cardiac anesthesia, and most of the topics related to thoracic anesthesia are presented elsewhere in this textbook. Therefore, the author will discuss only the most important problems occurring during combined thoracic and cardiac procedures.

1. Airway management. If pulmonary resection is performed before or after CPB the patient will require lung isolation. Detailed techniques and methods of choice are discussed in Chap. 16. The position of a double lumen tube or bronchial blocker should be always verified with a fiberoptic bronchoscope. If resection of pulmonary parenchyma is to be performed during CPB the patient can be intubated with standard, single lumen tube.
2. Management of hypoxemia during one lung ventilation is discussed in Chap. 6.
3. Transesophageal echocardiography (see Chap. 20). The use of TEE is one of the key components of intraoperative anesthetic management of patients undergoing combined cardiac and thoracic procedures. The important information obtained from intraoperative TEE during combined cardiac and thoracic procedures includes: assessment of left and right ventricular function (especially important after pneumonectomy), diagnosis of new wall-motion abnormalities (coronary artery bypass surgery), and evaluation of effects of valve repair/replacement.
4. The anesthesiologist and CPB. CPB has three main functions during cardiac procedures: (1) replacing the function of the heart (circulation of the blood), (2) replacing the function of the lungs (oxygenation and CO_2 removal), and (3) diversion of blood from the operating field to create optimal surgical conditions. To achieve these purposes superior and inferior vena cavae are cannulated and blood is passively drained into the CPB venous reservoir. The blood is then oxygenated and returned back to the patient via an aortic cannula usually placed in the distal part of the ascending aorta. In the case of combined thoracic-vascular surgery including the resection of the tumor invading the descending aorta one can use partial bypass, which diverts some of the blood from the left atrium and returns it back to one of the femoral arteries. Since the primary function of CPB is to oxygenate blood and perfuse the vital organs an important question for the anesthesiologist is what perfusion/oxygenation is optimal? Even though, it has been over 50 years since the first human use of extracorporeal circulation, there is no definite answer. Blood is exposed multiple times to the foreign surface of the extracorporeal circuit causing SIRS and microembolization, which can affect every organ of the human body. Apart from lung

injury, CPB can contribute to cognitive dysfunction, renal injury or failure, pancreatitis or, in the worst-case scenario, multiorgan dysfunction. It is the anesthesiologist's role to prevent or minimize these complications.

5. The anesthetic approach to combined procedures performed without the use of CPB. OPCABG is the preferred surgical management of coronary artery disease in patients who require pulmonary resection at the same time as coronary revascularization [20, 51, 53]. Revascularization is usually performed as the first part of the procedure followed by the resection of the pulmonary pathology. The most important principles of anesthetic management for OPCABG include aggressive maintenance of normothermia to prevent bleeding and/or acidosis, and preservation of hemodynamic stability during surgical manipulation of the heart. The first aim is achieved by the use of warming blankets, body warmers, fluid warmers, and adjustment of the room temperature in the operating theater. Maintaining hemodynamic stability is crucial for the ultimate success of the procedure, thus it requires ideal communication and cooperation between the surgeon and the anesthesiologist. It is accomplished by a combination of inotropic support, proper volume therapy (quite often achieved by "deep" Trendelenburg position) and antiarrhythmic prophylaxis. The surgeon should use gentle manipulations (e.g., incision of right pleura to avoid compression of the heart) and devices (e.g., Starfish™, Medtronic International Ltd., Minneapolis, MN) to preserve the geometry of the heart ventricles, their contractility, and prevent mitral regurgitation.
6. Hemodynamic support, right ventricular failure. Cardiac anesthesiologists must be familiar with all forms of circulatory support to provide hemodynamic stability during and after surgery. It can be achieved by optimization of pre- and after load, maintaining or improving contractility and preservation of a stable sinus rhythm. The most worrisome hemodynamic problem complicating combined cardiac-thoracic procedures is right ventricular dysfunction/failure. It is commonly caused by a rapid increase in the afterload (pressure) for the right side of the heart, especially after a major resection of the pulmonary parenchyma (e.g., pneumonectomy). The warning symptoms include right ventricular distension visualized directly by the surgeon and the anesthesiologist, a low cardiac output state, and a central venous pressure (CVP) higher than the pulmonary diastolic pressure (PAD). The treatments include:
 - Reduction of RV preload (e.g., promotion of diuresis with furosemide).
 - Maneuvers to decrease the pressure in the pulmonary circulation-hyperventilation, hyperoxia, and the pharmacological support. Among the intravenous agents, which decrease afterload for the RV and improve its contractility the first choices are dobutamine and milrinone. Inhalational pulmonary vasodilators (nitric oxide or prostacyclin) are used when a lack of response to intravenous agents occurs.

- Preservation of good perfusion pressure to the right ventricle and ventricular interdependence-norepinephrine or vasoressin, and/or the use of an intra-aortic balloon pump.
 - Since stroke volume is usually fixed in RV failure, to increase the cardiac output it is recommended to increase heart rate (e.g., A-V pacing).

7. Treatment of coagulopathy. Combined cardiothoracic procedures performed with the use of CPB are frequently complicated by excessive bleeding, which can have two possible causes: surgical and coagulopathy related to prolonged CPB. In cases of surgical resection of pulmonary parenchyma combined with a cardiac procedure, CPB duration often exceeds 2 h. Duration of CPB directly correlates with the magnitude of coagulopathy. There are multiple mechanisms of excessive, nonsurgical bleeding caused by extracorporeal circulation; among the most important are the dilutional effect, SIRS, platelet consumption, depleted amount of clotting factors, secondary fibrinolysis, and low hemoglobin. Treatment is based on the results of laboratory tests (INR, aPTT, fibrinogen level, and platelet count). Many centers use point-of-care devices, which deliver quick assessment of coagulation status based on results obtained from a whole-blood sample. Among the most popular ones are thromboelastography, sonoclot, and PFA-100. In our institution, for most of the combined cardiac-thoracic cases we secure at least two, large bore venous catheters to be able to transfuse, large volumes of blood products in relatively short period of time.

Summary

There is no complete agreement about the optimal surgical management of patients who are suffering from both cardiac and thoracic diseases requiring surgery [1, 49, 59]. The arguments for one-stage procedures are avoidance of a second surgery/anesthetic and reduced hospital stay and cost. However, two-stage procedures may be associated with less surgical trauma and blood loss, and may offer better long-term survival because the consequences of CPB are minimized.

Combined cardiac–thoracic procedures should be performed only for selected cases in centers which have an expertise in both cardiac and thoracic anesthesia and surgery. This chapter briefly describes the important perioperative considerations and management. Since there is minimal literature describing the anesthetic management for combined cardiac–thoracic procedures the aforementioned recommendations are based on the experience and clinical practice developed in the institution where the author works.

Clinical Case Discussion

Case: A 21-year-old patient admitted for redo cardiac surgery for resection of recurrent left atrial angiosarcoma invading pulmonary tissue which was demonstrated on a

recent follow-up chest X-ray and CT scan of his chest (see Figs. 32.6 and 32.7). The proposed procedure will also involve resection of pulmonary parenchyma. His previous surgery was performed 3 years ago without complications and followed by multiple courses of chemotherapy. He has no other significant comorbidities. The anesthesiologist is asked to decide whether the patient will tolerate a combined cardiac–thoracic procedure and what additional tests he/she would like preoperatively.

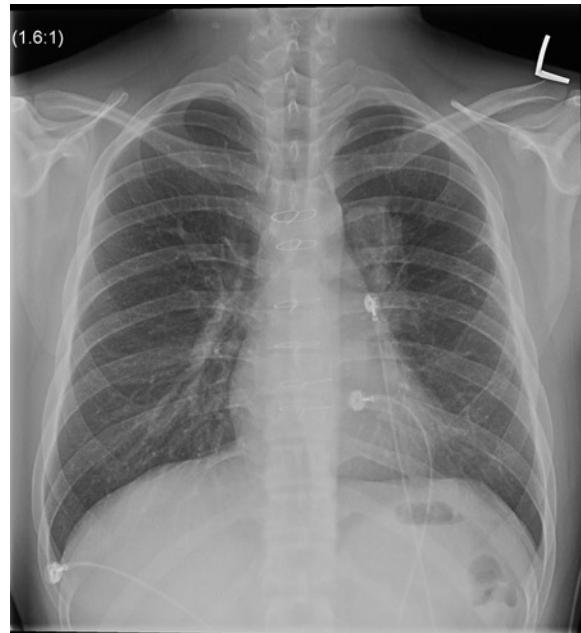


FIG. 32.6. Chest X-ray taken before surgery.

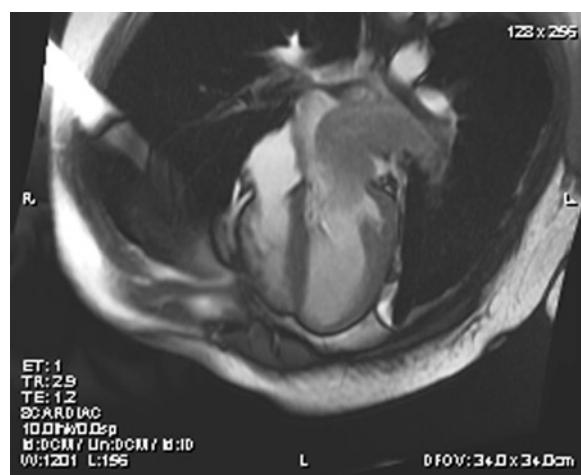


FIG. 32.7. Computed tomogram showing invasion of the tumor obtained before surgery.

Questions

- What additional tests would you order?
- Will the patient tolerate procedure? What kind of thoracic procedure will the patient require to achieve complete eradication of his tumor?
- What is your anesthetic plan?
- Do you have any specific concerns related to intraoperative management?
- What kind of postoperative complications can you expect?

Figures 32.8 and 32.9

These pictures show the intraoperative transesophageal echo findings.

Questions

- What cardiac procedure should be performed?
- Which pulmonary vein(s) are invaded?
- What postoperative complications would you expect?

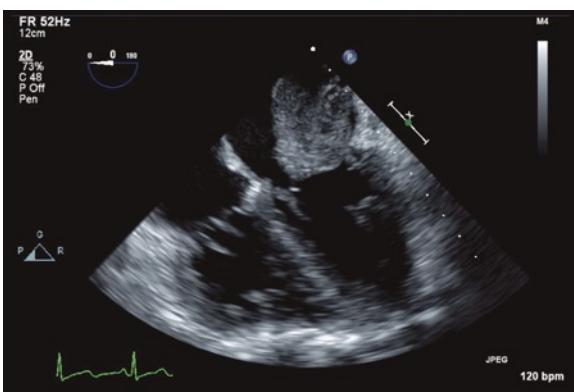


FIG. 32.8. Picture obtained during intraoperative transesophageal examination. Mid-esophageal, four chamber view.

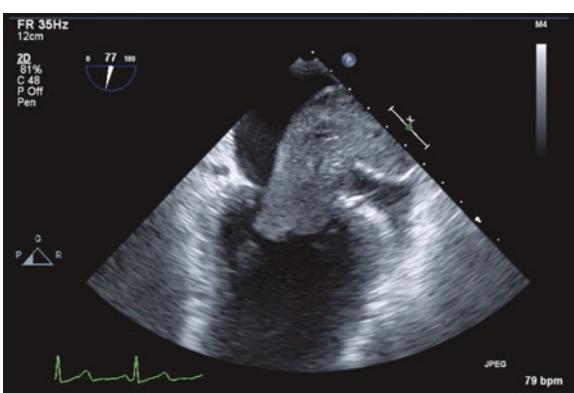


FIG. 32.9. Picture obtained during intraoperative transesophageal examination. Mid-esophageal, two chamber view.

Answers

Before proceeding with combined cardiac-thoracic procedure additional tests should be ordered: pulmonary function test (PFT) (possible left-sided pneumonectomy) and echocardiography to reassess the extension of the tumor and its mobility. As mentioned, to achieve full surgical resection of the recurrent neoplastic lesion, the patient most likely will require a left pneumonectomy. Assuming that the PFTs are acceptable, and knowing that the patient has no other significant comorbidities, the patient should tolerate a combined procedure. Most likely, the procedure will involve left atrial resection and left pneumonectomy with the use of CPB. Additionally, following left atrial resection, atrial reconstruction with bovine pericardium will be necessary. This will result in a long CPB time complicated by coagulopathy and massive blood loss. Appropriate venous access must be secured (at least, two large-bore, peripheral venous catheters, and central venous access), a sufficient supply of blood products must be available. Even though the pneumonectomy will be performed during CPB, the postoperative course might be complicated by prolonged mechanical ventilation. One might decide to use double lumen tube for intubation to protect the bronchial stump during prolonged use of mechanical ventilation.

Unfortunately, following such an extensive, combined surgery the patient may suffer from a wide spectrum of postoperative complications occurring after cardiac and thoracic procedures.

Among the most serious are:

- Coagulopathy and transfusion of large amounts of blood products with all subsequent complications (e.g., renal failure, transfusion-related lung injury)
- Prolonged mechanical ventilation
- Low-cardiac output syndrome
- Postpneumonectomy pulmonary edema
- Broncho-pleural fistula

The presented echocardiograms show tumor originating from left upper pulmonary vein, thus the patient will require a left pneumonectomy. Additionally, tumor is invading the mitral valve, therefore the procedure should be expanded to include mitral valve replacement. Most likely almost all the left atrium must be fully resected and reconstructed.

References

1. Slinger PD, Chang DCH, David TE, editors. Perioperative care in cardiac anesthesia and surgery. Philadelphia: Lippincott Williams & Wilkins; 2006;43–8.
2. Rao V, Todd TRJ, Weisel RD, et al. Results of combined pulmonary resection and cardiac operation. Ann Thorac Surg. 1996;62:342–7.
3. Ciriacio P, Carretta A, Calori G, Mazzone P, Zannini P. Lung resection for cancer in patients with coronary artery disease: analysis of short term results. Eur J Cardiothorac Surg. 2002;22:35–40.

4. Wąsowicz M, Biczysko W, Marszałek A, Yokoyama S, Nakayama I. Ultrastructural studies on selected elements of the extra cellular matrix in the developing rat lung alveolus. *Folia Histochem Cytopiol*. 1998;36:3–13.
5. Wąsowicz M, Kashima K, Yokoyama S, Nakayama I. Pulmonary surfactant migrates into the alveolar capillaries of newborn rats an immunolectron microscopic study. *Acta Anat*. 1996;156:11–21.
6. Wąsowicz M, Biczysko W. In: Andres J, Wąsowicz M, editors. Selected problems of anesthesia and critical care in cardiovascular surgery. Kraków: Danbert; 2002;174–89.
7. Wąsowicz M, Drwiła R, Biczysko W, Marszałek A, Florek E, Andres J. Effects of exogenous surfactant on alveolar barrier. An experimental study. *Anaesth Inten Ther*. 2002;34:76–80.
8. Wąsowicz M, Sobczyński P, Szulc R, Biczysko W. Ultrastructural changes in the lung alveoli after cardiac surgical operations with the use of cardiopulmonary bypass (CPB). *Pol J Pathol*. 1999;50:189–96.
9. Ng CSH, Wan S, Yim APC, Arifi AA. Pulmonary dysfunction after cardiac surgery. *Chest*. 2002;121:1269–77.
10. Biczysko W, Wąsowicz M, Marszałek A. Stromal compartment in the developing lung's alveoli – an electron microscopic study. *Clin Perinat Gynaecol*. 1994;6:107–19.
11. Wąsowicz M, Biczysko W, Sobczyński P. Structure and activity of pulmonary surfactant and their implications for intensive therapy. *Inten Care Emerg Med*. 1998;1:35–44.
12. Biczysko W, Wąsowicz M, Metzner J, Marszałek A. In: Drobnik L, Jurczyk W, editors. Problems of anesthesiology and intensive therapy. Warszawa: Wydawnictwo Lekarskie PZWL; 1998;96–109.
13. Biczysko W, Marszałek A, Wąsowicz M. Maturation of lung epithelia in transmission electron microscopic study. *Clin Perinat Gynaecol*. 1993;3:3–23.
14. Doyle I, Nicholas TE, Bernste AD. Serum surfactant protein A levels in patients with acute cardiogenic pulmonary edema and adult respiratory distress syndrome. *Am J Respir Crit Care Med*. 1995;152:307–17.
15. Sobczyński P, Wąsowicz M. In: Zapalski S, Checinski P, editors. Clinical aspects of lung reperfusion. Clinical aspects of ischemia and reperfusion. Bielsko Biała: Alfa Medica Press; 1997;79–89.
16. Wąsowicz M, Yokoyama S, Kashima K, Nakayama I. The connective tissue compartment in the terminal region of the developing rat lung. *Acta Anat*. 1996;156:268–82.
17. Biczysko W, Wąsowicz M, Marszałek A, Florek E. Why do the lungs of premature newborns function improperly? A morphological study of the connective tissue and vascular compartments in the developing lung. *Arch Perinat Med*. 1999;5:19–26.
18. Danton MHD, Anikin VA, McManus KG, McGuigan JA, Campanali G. Simultaneous cardiac surgery with pulmonary resection: presentation of series and review of literature. *Eur J Cardiothorac Surg*. 1998;13:667–72.
19. Wiebe K, Baraki H, Macchiarini M, Haverich A. Extended pulmonary resections of advanced thoracic malignancies with support of cardiopulmonary bypass. *Eur J Cardiothorac Surg*. 2006;29:571–8.
20. Dyszkiewicz W, Jemielity M, Piwkowski C, et al. The early and late results of combined off-pump coronary artery bypass grafting and pulmonary resection in patients with concomitant lung cancer and unstable coronary heart disease. *Eur J Cardiothorac Surg*. 2008;34:531–5.
21. Spaggiari L, D'Aiuto M, Veronesi G, et al. Extended pneumonectomy with partial resection of the left atrium, without cardiopulmonary bypass for lung cancer. *Ann Thorac Surg*. 2005;79:234–40.
22. Voets AJ, Sheik Joesoef K, van Teeffelen MEJM. Synchronously occurring lung cancer (stages I-II) and coronary artery disease: concomitant versus staged surgical approach. *Eur J Cardiothorac Surg*. 1997;12:713–7.
23. Wąsowicz M. In: Andres J, Wąsowicz M, editors. Selected problems of anesthesia and critical care in cardiovascular surgery. Kraków: Danbert; 2002;191–207.
24. Clark SC. Lung injury after cardiopulmonary bypass. *Perfusion*. 2006;21:225–8.
25. Weissman C. Pulmonary complications after cardiac surgery. *Semin Cardiothorac Vasc Anesth*. 2004;8:185–211.
26. Picone AL, Lutz CJ, Finck C, et al. Multiple sequential insults cause post-pump syndrome. *Ann Thorac Surg*. 1999;67:978–85.
27. Wąsowicz M, Drwiła R, Sobczyński P, Przybyłowski P, Dziatkowiak A. Lung alveolar damage during coronary artery bypass grafting with use of cardiopulmonary-bypass: and old nemesis? *Br J Anaesth*. 2000;84(Suppl 1):18.
28. Wąsowicz M, Sobczyński P, Drwiła R, Biczysko W, Marszałek A, Andres J. Air-blood barrier injury during cardiac operations with the use of cardiopulmonary bypass (CPB). An old story? *Scand Cardiovasc J*. 2003;37:216–21.
29. Tonz M, Milhajevic T, Von Segesser LK. Acute lung injury during cardiopulmonary bypass. Are the neutrophils responsible? *Chest*. 1995;108:1551–56.
30. Kotani N, Hashimoto H, Sessler DI, et al. Neutrophil number and interleukon -8 and elastase concentration in bronchoalveolar lavage fluid correlate with decreased arterial oxygenation after cardiopulmonary bypass. *Anesth Analg*. 2000;90:1046–51.
31. Kotani N, Hashimoto H, Sessler DI, et al. Cardiopulmonary bypass produces greater pulmonary than systemic proinflammatory cytokines. *Anesth Analg*. 2000;90:1039–45.
32. Sinclair DG, Haslam PL, Quinlan GL, Pepper JR, Evans TW. The effects of cardiopulmonary bypass on interstitial and pulmonary endothelial permeability. *Chest*. 1995;108:718–24.
33. Kawamura T, Wakusawa R, Okada K, Inada S. Elevation of cytokines during open heart surgery with cardiopulmonary bypass: participation of interleukin 8 and 6 in reperfusion injury. *Can J Anesth*. 1993;40:1016–21.
34. Chenoweth DE, Cooper SW, Hugli TE, et al. Complement activation during cardiopulmonary bypass. Evidence for generation C3a and C5a anaphylatoxins. *N Engl J Med*. 1981;304:497–503.
35. Warner AE. Pulmonary intravascular macrophages. Role in acute lung injury. *Clin Chest Med*. 1996;17:125–35.
36. Royston D, Fleming JS, Desai JB, et al. Increased production of peroxidation products associated with cardiac operations. Evidence for free radical generation. *J Thorac Cardiovasc Surg*. 1986;91:75–766.
37. Wąsowicz M, Drwiła R, Jeleń H, Przybyłowski P, Andres J, Dziatkowiak A. Lipid peroxidation (LO) during cardiac operations with use of cardiopulmonary bypass measured by headspace chromatography. *Eur J Anaesth*. 2001;18 Suppl 22:19.
38. Rady MY, Ryan T, Star NY. Early onset of acute pulmonary dysfunction after cardiovascular surgery; risk factors and clinical outcomes. *Crit Care Med*. 1997;25:1831–9.

39. Magnusson L, Zemgulis V, Wicky ZS, Tyden H, Thelin S, et al. Atelectasis is a major cause of hypoxemia and shunt after cardio-pulmonary bypass. *Anesthesiology*. 1997;87:1153–63.
40. Bouza E, Perez A, Munoz P, et al. Ventilator-associated pneumonia after heart surgery: a prospective analysis and the value of surveillance. *Crit Care Med*. 2003;31:1964–70.
41. Gaynes R, Bizek B, Movry-Hanley J, et al. Risk factors for nosocomial pneumonia after coronary artery bypass operations. *Ann Thorac Surg*. 1991;51:215–8.
42. Karkouti K, Wijeysundera DN, Yau TM, et al. The independent association of massive blood loss with mortality in cardiac surgery. *Transfusion*. 2004;44:1453–62.
43. Taggard DP. Respiratory dysfunction after cardiac surgery: effect of avoiding cardiopulmonary bypass and the use of bilateral internal mammary artery. *Eur J Cardiovasc Surg*. 2000;18:31–7.
44. Richter JA, Meisner H, Tassani P, et al. Drew-Anderson technique attenuates systemic inflammatory response syndrome and improves respiratory function after coronary artery bypass grafting. *Ann Thorac Surg*. 2000;69:7783.
45. Minkovich L, Djaiani G, Katznelson R, et al. Effects of alveolar recruitment on arterial oxygenation in patients after cardiac surgery: a prospective, randomized, controlled clinical trial. *J Cardiothorac Vasc Anesth*. 2007;21:375–8.
46. Tassani P, Richter P, Barankay A, et al. Does high-dose methylprednisolone in aprotinin-treated patients attenuates the systemic inflammatory response during coronary artery bypass grafting procedures? *J Cardiothorac Vasc Anesth*. 1999;13:165–72.
47. Saxena P, Tam RKW. Combined off-pump coronary artery bypass surgery and pulmonary resection. *Ann Thorac Surg*. 2004;78:498–501.
48. Ng CSH, Arifi AA, Wan S, Wai S, Lee TW, Yim APC. Cardiac operation with associated pulmonary resection: a word of caution. *Asian Cardiovasc Thorac J*. 2002;10:362–4.
49. Klepetko W. Surgical intervention for T4 lung cancer with infiltration of the thoracic aorta: are we back to the archetype of surgical thinking? *J Thorac Cardiovasc Surg*. 2005;129:727–9.
50. De Perrot M, Fadel ZE, Mussot S, de Palma A, Chapelier A, Darteville P. Resection of locally advanced (T4) non-small cell lung cancer with cardiopulmonary bypass. *Ann Thorac Surg*. 2005;79:1691–7.
51. Dyszkiewicz W, Jemielity MM, Piwkowski CT, Perek B, Kasprzyk M. Simultaneous lung resection for cancer and myocardial revascularization without cardiopulmonary bypass (off-pump coronary artery bypass grafting). *Ann Thorac Surg*. 2004;77:1023–7.
52. Mariani M, von Boven W, Duurkens VAM, et al. Combined off-pump coronary surgery and right lung resections through midline sternotomy. *Ann Thorac Surg*. 2001;71:1342–4.
53. Marcucci C, Chassot P-G, Gardaz J-P, Magnusson L, et al. Fatal myocardial infarction after lung resection in a patient with prophylactic preoperative coronary stenting. *Br J Anaesth*. 2004;92:743–7.
54. Shudo Y, Takahashi T, Ohta M, et al. Radical operation for invasive thymoma with intracaval, intracardiac and lung invasion. *J Card Surg*. 2007;22:330–2.
55. Nakajima J, Morota T, Matsumoto J, et al. Pulmonary intimal sarcoma treated by a left pneumonectomy with pulmonary arterioplasty under cardiopulmonary bypass: report of case. *Surg Today*. 2007;37:496–9.
56. Venuta F, Ciccone AM, Anile M, et al. Reconstruction of the pulmonary artery for lung cancer: long-term results. *J Thorac Cardiovasc Surg*. 2009;138:1185–91.
57. Ratto GB, Costa R, Vassallo G, et al. Twelve-year experience with left atrial resection in the treatment of non-small cell lung cancer. *Ann Thorac Surg*. 2004;78:234–7.
58. La Francesca S, Frazier OH, Radovancevic B, De Caro LF, Reul GJ, Cooley DA. Concomitant cardiac and pulmonary operations for lung cancer. *Tex Heart Inst J*. 1995;22:296–300.
59. Lennon PF, Hartigan PM, Friedberg JS. Clinical management of patients undergoing concurrent cardiac surgery and pulmonary resection. *J Cardiothorac Vasc Anesth*. 1998;12:587–90.

Anesthetic Considerations for Infectious, Congenital, and Acquired Pulmonary Disorders

Peter Slinger and Rebecca Jacob

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Key Points

- The risk of contamination of healthy lung regions from infected secretions in patients with infectious processes such as lung abscess, cyst, bronchopleural fistula, etc.
- The risk of tension pneumothorax during positive pressure ventilation with bronchopleural fistula or bullae.
- The risk of inability to ventilate due to air leak with bronchopleural fistula.
- The increased risk of intraoperative hemorrhage due to intrathoracic inflammation and scarring with infectious diseases.
- The possibility of sepsis developing before or during surgery with infectious diseases.
- The presence of right-to-left shunt in patients with pulmonary arteriovenous malformations.

Bronchopleural Fistula

Air leaks from the lung into the pleural space are classified according to several different systems (see Table 33.1). An anatomic classification is based on the site of the communication between the respiratory system and the pleura. An alveolar-pleural fistula (APF) is a communication between the pulmonary parenchyma distal to a segmental bronchus and the pleural space, while a bronchopleural fistula (BPF) is a communication between a main stem, lobar, or segmental bronchus and the pleural space [1]. Most air leaks after pulmonary resection are APFs. APFs rarely require reoperation. BPFs have significant morbidity and almost always require some form of surgical intervention.

Another classification of air leaks is functional and depends on the phase of the respiratory cycle and the amount of gas lost

TABLE 33.1. Classification of lung air leaks.

Anatomical

1. *Alveolar-pleural fistula* (APF): Pulmonary parenchyma-pleural communication distal to a segmental bronchus. Common after pulmonary resections (except pneumonectomy). Rarely requires surgery
2. *Bronchopleural fistula* (BPF): Communication between a main stem, lobar, or segmental bronchus and the pleura. Usually requires some type of surgical intervention

Functional

1. *Continuous*: Usually during mechanical ventilation with a BPF. Uncommon
2. *Inspiratory*: Usually during mechanical ventilation with a sizable APF or small BPF
3. *Expiratory*: Common after pulmonary resections due to an APF
4. *Forced expiratory*: Only during coughing. Common postlung resection due to a small APF

through the leak [2]. The largest gas loss is from a continuous leak, which is present throughout the respiratory cycle. This is the least common type of air leak and is seen in patients receiving mechanical ventilation with a BPF. The second largest type is an inspiratory air leak seen almost exclusively in the patient receiving mechanical ventilation with a sizable APF or a small BPF. The third largest leak is an expiratory leak which is present only during expiration. This type of leak is commonly seen after pulmonary surgery and is usually due to an APF. A fourth type of leak is referred to as a forced air leak and is present only with coughing. This type of leak is also common after pulmonary resection. Postoperatively small leaks resolve more quickly with simple underwater seal drainage but larger leaks require suction [3].

A BPF may be caused by: (1) rupture of a lung abscess, bronchus, bulla, cyst, or parenchymal tissue into the pleural space, (2) the erosion of a bronchus by carcinoma or chronic inflammatory disease (see Fig. 33.1), or (3) stump dehiscence of a bronchial suture line after pulmonary resection. Pneumonectomy patients have an incidence of BPF, ranging from 2 to 11% [4] with a mortality ranging from 5 to 70%. BPF is more common with preoperative infection and after chemotherapy [5].

The diagnosis of BPF is usually made clinically. In the early postoperative period after pneumonectomy, the diagnosis is based on the sudden onset of dyspnea, subcutaneous emphysema, contralateral deviation of the trachea, and a decrease of the fluid level on serial radiographs of the chest [6]. Early postpneumonectomy BPF is often life threatening since the mediastinum is still mobile. Pendeluft, or ineffective exchange of gas, occurs between the remaining lung and the postsurgical hemithorax, similar to the situation of a flail chest in trauma. If the disruption occurs early in postpneumonectomy patients, it is possible to resuture the stump. Late or chronic postpneumonectomy bronchial disruption presents subacutely with fever and cough and is not usually life threatening because the mediastinum has become fixed due to fibrosis and gas exchange remains adequate in the nonoperative hemithorax. Late postpneumonectomy BPF is usually managed initially with drainage or with a Clagett procedure (see Chap. 45) [7] which allows for sterilization of the pleural space with packing



FIG. 33.1. Coronal chest CT scan of a patient with bilateral upper lobe bronchopleural fistulae due to *Aspergillus* infection. Surgical management was with two separate lobectomies. Airway management for the initial left thoracotomy and upper lobectomy was with a left-sided double-lumen tube (DLT) placed in the right bronchus intermedius, excluding the right upper lobe. The airway management for the subsequent right upper lobectomy was with a left-sided DLT in the left mainstem bronchus.

and antibiotic instillations. Following this, a secondary closure may be performed using a muscle or omental flap to reinforce the bronchial stump.

In postlobectomy patients, persistent air leak, purulent drainage, and expectoration of purulent material are usually diagnostic indicators of a BPF. When the fistula appears after removal of a chest tube, the diagnosis of BPF is made on the basis of fever and a new air-fluid level in the pleural cavity on the chest radiograph. A surgical drainage procedure such as an Eloesser flap may then be required (see Fig. 33.2).

Diagnosis is most often confirmed by bronchoscopic examination. Additionally, bronchography and sinograms of the fistula may be used to confirm the diagnosis. Other diagnostic methods include the injection of an indicator, such as methylene blue, into the pleural space and subsequent recovery from sputum. Accumulation of radionuclide in the pleural space after inhalation of xenon or a mixture of O₂ and N₂O to detect the presence of a BPF can also be used as indicators [8]. In nonpneumonectomy cases, if the lung expands to fill the thoracic cavity, the air leak can usually be controlled with chest tube drainage alone. However, if the fistula is large and a significant leak through a large persistent pleural space occurs, it is unlikely that the fistula will close, and surgical resection is necessary. With small persistent leaks or in debilitated patients

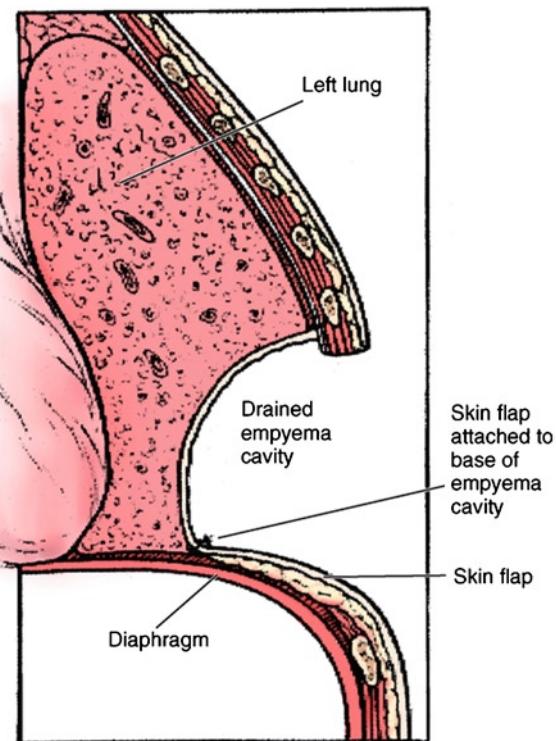


FIG. 33.2. Diagram of a Clagett procedure as a first stage operation to treat a chronic infectious process in the chest. There are many variations of this surgical procedure shown here for a chronic empyema. The skin is sutured to the parietal pleura to prevent closure of wound and to ensure drainage (this figure was published in Pearson's Thoracic and Esophageal Surgery, 3rd ed. Patterson GA. Pleura. p. 1168. © Elsevier 2008).

several endoscopic methods of treating BPFs have been described such as the use of fibrin glue, bronchial stents, or endobronchial valves [9].

Anesthetic Management

The patient with a BPF presents several intraoperative challenges for the anesthesiologist (see Table 33.2), these include: (1) the need for lung isolation to protect healthy lung regions, (2) the possibility of tension pneumothorax with positive pressure ventilation, and (3) the possibility of inadequate ventilation due to air leak across the fistula. Except in the rare acute indication for surgery, every effort possible should be made to eliminate active respiratory infection preoperatively, with appropriate antibiotics and aggressive chest physiotherapy including postural drainage.

It is useful to estimate the loss of tidal volume through the BPF, which may be done in two ways. First, one should determine whether air bubbles flow intermittently or continuously through the chest tube. If air bubbles flow intermittently, then the fistula is small. In contrast, when a patient has a large BPF or bronchial rupture, air will bubble continuously through the water-seal chamber of the chest tube drainage system.

TABLE 33.2. Anesthetic considerations in a patient with a bronchopleural fistula.

- Lung isolation to prevent soiling of healthy lung regions from potentially infected secretions via the BPF
- Prevention of tension pneumothorax during positive pressure ventilation
- Possible inadequate ventilation due to loss of inspired volume through the BPF

Second, the size of the BPF may be quantified by the difference between inhaled and exhaled tidal volumes. In a nonintubated patient, this may be determined with a tight-fitting mask and a fast-responding spirometer. In an intubated patient, it is determined by direct attachment of a spirometer to the endotracheal tube (ETT). The larger the air leak, the greater the need to isolate the BPF with the use of a lung isolation device, either a double-lumen tube (DLT), single-lumen endobronchial tube, or independent bronchial blocker.

Several nonsurgical approaches (i.e., the use of various mechanical ventilation-chest tube drainage systems) have been used for the treatment of patients with a BPF. These approaches consist of OLV and differential lung ventilation, including high frequency ventilation (HFV), PEEP to the pleural cavity equal to intrathoracic PEEP, and unidirectional chest tube values.

For patients undergoing operative repair, the ability to adequately deliver positive-pressure ventilation intraoperatively must be carefully considered prior to surgery. A chest drain should be placed prior to induction to avoid the possibility of tension pneumothorax with positive pressure ventilation. If a fistula is small, chronic, and uninfected, a single-lumen ETT can be used safely. If the air leak is significant, then a DLT is the best choice for delivering positive-pressure ventilation (see Table 33.3). The DLT can provide positive pressure ventilation to the normal lung without loss of minute ventilation through the fistula and prevent the contamination of the uninfected lung with infected material when the patient is turned to the lateral decubitus position. In an emergency, an uncut single-lumen tube or a specifically designed endobronchial tube can be advanced into the contralateral mainstem bronchus. This will not allow for suctioning of the fistula side and will block the right upper lobe when placed in the right mainstem bronchus. However, it will provide for protection of the nonoperative lung and ensure gas exchange. In nonpneumonectomy patients, a bronchial blocker can also be placed through an ETT into the mainstem bronchus on the side of the fistula for lung isolation. Blockers are less stable and thus offer less protection to the noninvolved lung than double- or single-lumen endobronchial tubes. After a pneumonectomy, blockers are not an option due to the short length of the bronchial stump.

For all patients with a BPF, induction of anesthesia should be done with a slight head-up position and lateral tilt, with the good lung up, to minimize contamination of the good lung until lung isolation is secured. Options for anesthetic

TABLE 33.3. Options for airway management with a bronchopleural fistula.

Technique	Pro	Con
Double-lumen tube	<ul style="list-style-type: none"> Most secure method of isolation Allows for easy bilateral suctioning and ventilation Differential lung ventilation possible 	<ul style="list-style-type: none"> Most difficult to place in an awake patient
Single-lumen endobronchial tube	<ul style="list-style-type: none"> Standard endotracheal tubes are readily available 	<ul style="list-style-type: none"> Does not allow for easy suctioning or ventilation of BPF lung Standard single-lumen tubes not well designed for endobronchial use Specifically designed endobronchial tubes not widely available Placed in R main bronchus will block the R upper lobe
Bronchial blocker	<ul style="list-style-type: none"> Can be deflated to suction or ventilate the BPF side as needed Allows for lobar isolation 	<ul style="list-style-type: none"> Least secure method of lung isolation

TABLE 33.4. Anesthetic management options with a major bronchopleural fistula.

- Awake fiberoptic intubation with a single-lumen or double-lumen endobronchial tube or bronchial blocker. Induction of general anesthesia after lung isolation
- Induction of general anesthesia maintaining spontaneous ventilation during intubation, avoiding positive pressure ventilation until lung isolation is secured
- Modified rapid sequence induction, avoiding or limiting positive pressure ventilation until lung isolation is confirmed
- Regional anesthesia

management with a BPF are presented in Table 33.4. The safest method of obtaining lung isolation is awake fiberoptic intubation with a DLT or single-lumen tube advanced into the contralateral mainstem bronchus [10]. This requires a cooperative patient and excellent topical anesthesia and is often not an option. Another option is to maintain spontaneous ventilation during induction and intubation until lung isolation is secured. This decreases the possibility of inadequate positive pressure ventilation due to air leak, but is not well tolerated in older patients with significant comorbidity and is not a good option in a patient with a full stomach. If the patient has a postpneumonectomy fistula, the DLT or single-lumen endobronchial tube must be guided under direct vision with the assistance of fiberoptic bronchoscopy, and the tip of the endobronchial lumen should be placed in the existing lung (i.e., for right-sided fistula a left-sided tube). A useful management plan is a modified rapid sequence induction with a bronchoscope placed in the single- or DLT during intubation and avoidance of positive pressure ventilation until lung isolation is achieved [11]. During induction of anesthesia, suction of the chest tube should be discontinued to decrease the loss of tidal volume with the initiation of positive-pressure ventilation. After the chest is opened, if an excessive leak is encountered when using a single-lumen ETT, ventilation can be improved by lung packing and manual control of the air leak.

In the patient with a chronic BPF, there are many options to manage anesthesia if the risks of contralateral soiling are minimal. Endoscopic procedures, including rigid bronchoscopy, can be performed with spontaneous ventilation [12].

This is a viable option in younger patients but older patients with significant comorbidities may not tolerate the respiratory or hemodynamic depressant effects of a prolonged deep anesthetic while maintaining adequate spontaneous ventilation. An option to avoid instrumentation of the airway in elderly patients with a BPF after pneumonectomy is the use of thoracic epidural anesthesia combined with awake intravenous sedation during minimally invasive surgery [13]. Another alternative method of ventilating patients with a BPF is the use of HFV or high frequency oscillation (HFO) possibly with permissive hypercapnia. This avoids barotrauma to the nonoperative lung, decreases BPF air leak, and optimizes the operative outcome [14]. The advantage of high-frequency oscillatory ventilation over conventional mechanical ventilation is that it uses lower peak airway pressures and higher mean airway pressures and may decrease the air leak across the fistula. HFV has been used in combination with spontaneous ventilation for endoscopic BPF repair in a patient with a chronic postpneumonectomy fistula [15].

In all cases of general anesthesia for a BPF, at the end of surgery and prior to extubation, the airways on both sides should be carefully examined with fiberoptic bronchoscopy. Specifically the affected side needs to be suctioned for remaining secretions/pus. With a DLT this should be performed before the bronchial cuff is deflated. Early extubation in the operating room should be attempted in all patients undergoing fistula repair to avoid barotrauma to the surgical stump from positive pressure ventilation in the postoperative period.

Postoperative Management

When a patient with a BPF requires postoperative ventilation the optimal method of ventilation will depend on the individual physics of the air leak across the fistula. The volume of air leak across a fistula will depend on the size of the fistula(s) and the location and the pressure differential between the mean airway pressure and the pleural space at the site of the fistula. Each of these variables will be different in different patients and the common goal is to maintain adequate gas exchange while limiting the volume of air leak and both need to be closely monitored. In addition to conventional methods

of positive pressure ventilation, HFV and HFO techniques have been useful in certain individuals. Generally, high frequency techniques have been useful with proximal (tracheal or main bronchial) fistulas and in patients with normal lung parenchyma [16]. The physics may be that HFV techniques tend to produce lower proximal mean airway pressures than conventional techniques and result in less air leak with central BPFs. However, HFV may be associated with higher distal mean airway pressures and a larger air leak with distal BPFs. Similarly, chest-drain suction management with a BPF requires individualization. Suction may be required to prevent a tension pneumothorax or lung collapse but may also increase the cross-fistula leak.

In refractory respiratory failure with a BPF, independent lung ventilation using a DLT may be required. The techniques of ventilation to the two lungs can be adjusted independently to minimize air leak and optimize gas exchange [17]. Lobar blockade with a bronchial blocker in addition to independent lung ventilation with a DLT has also been reported [18].

Bronchiectasis

Bronchiectasis is a chronic condition of localized, irreversible dilatation of part of the bronchial tree. Involved bronchi are dilated, inflamed, and easily collapsible, resulting in airflow obstruction and impaired clearance of secretions. Bronchiectasis is associated with a wide range of disorders, but it usually results from necrotizing bacterial infections. Bronchiectasis was a common respiratory problem in the preantibiotic era and continues to be a problem in third world countries (see “Thoracic Anesthesia in Developing Countries” at the end of

this chapter). In developed countries it is now mainly seen in congenital conditions which result in impaired clearance of bronchial secretions such as cystic fibrosis or other forms of respiratory ciliary dysmotility. Kartagener's syndrome is a congenital ciliary dysmotility syndrome that encompasses bronchiectasis, infertility, and dextrocardia or situs inversus and may include chronic sinusitis and otitis media [19]. Bronchiectasis may also develop distal to a chronic partial bronchial obstruction from a tumor or foreign body.

The diagnosis is suggested by the history of hemoptysis or recurrent lower respiratory infections and cough productive of chronic purulent secretions. The cough is often related to a change of position. Diagnosis is confirmed by imaging (see Fig. 33.3a, b) and bronchoscopy. Bronchiectasis may require surgery if it causes massive hemoptysis or recurrent pneumonia. Surgical procedures involve resection of the involved bronchiectatic segments or lobes. Long-term survival has been reported after resection of up to 13 lung segments for bronchiectasis (there are only 19 lung segments in total) [20]. For severe bilateral forms of bronchiectasis, bilateral lung transplantation may be the only possible surgical option.

The principles of anesthetic management for bronchiectasis are similar to the concerns mentioned above for protection of healthy lung regions from the secretions in the affected lung in cases of BPF (see Table 33.5). There is not the concern for loss of ventilation or tension pneumothorax that occurs with BPF so there is no caveat attached to positive pressure ventilation in bronchiectasis. As for BPF, induction of anesthesia should be performed in a position that limits spread of secretions until lung isolation is achieved; this most commonly is a slight head-up position with the infected lung dependent. It is best to initially place as large a single-lumen ETT as possible

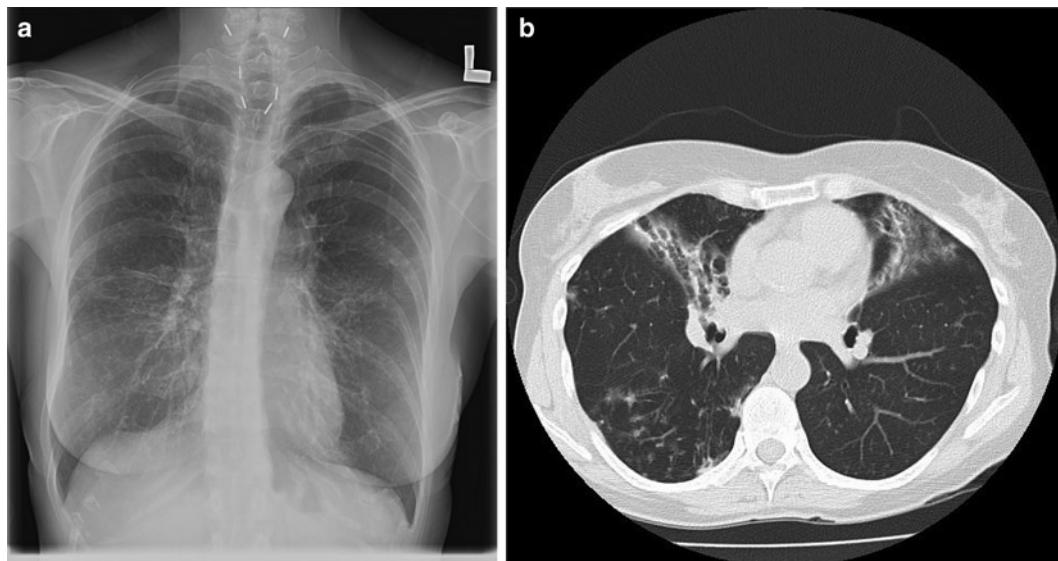


FIG. 33.3. (a) Chest X-ray and (b) chest CT scan of a patient with severe bilateral bronchiectasis predominately affecting the lower lobes. There is extensive bronchial thickening and dilation with evidence of mucoid impaction. The left lower lobe is atelectatic. Oxygen tubing can be seen in the chest X-ray. This patient has a ciliary dysmotility syndrome of unknown etiology. A peripheral central infusion cannula and clips from previous thyroid surgery can be seen on the chest X-ray.

TABLE 33.5. Principles of anesthetic management for bronchiectasis and other infectious respiratory lesions.

- Appropriate preoperative antibiotic therapy
- Aggressive preoperative chest physiotherapy and postural drainage
- Induction of anesthesia in a position to minimize contamination of healthy lung segments (e.g., slight head-up with infected lung dependent)
- Initial airway management with a large single-lumen tube for fiberoptic bronchoscopy and thorough tracheobronchial toilette
- Lung isolation with a double-lumen tube prior to repositioning the patient for surgery
- Increased risk of intraoperative hemorrhage

and to perform careful fiberoptic suctioning and segmental lavage of the secretions in the infected lung segments. The single-lumen tube can then be replaced with a DLT and after lung isolation and inflation of the bronchial cuff, the patient can be repositioned with the noninfected lung dependent for surgery. The use of a bronchial blocker or single-lumen tube for lung isolation in bronchiectasis is not ideal since the protection of the healthy lung is less secure. However, these airway options may be required in certain circumstances such as the patient with a difficult airway. Protecting ipsilateral lung segments intraoperatively from infected secretions is complicated and is usually not necessary after initial thorough airway toilette through a single-lumen tube. If indicated, lobar blockade can be performed by several methods depending on the site of the diseased segments. The left or right upper lobes can be deliberately obstructed by a left-sided double lumen placed in the ipsilateral mainstem bronchus with fiberoptic bronchoscopic guidance. The lower or right-middle lobe bronchi can be packed with saline soaked gauze during rigid bronchoscopy at induction, the gauze is then removed when the bronchus is opened later during thoracotomy.

The use of neuraxial anesthetic techniques, specifically thoracic epidural analgesia in bronchiectasis and other infectious indications for thoracic surgery is a more complex clinical question than in other types of pulmonary resection due to the extremely small possibility of contamination and epidural abscess in the patient with an infectious process. Each case will require an individual risk/benefit assessment and discussion between the patient and/or family and the anesthesiologist. In most cases, for a patient who is not septic and has significant pulmonary disability, the risks are acceptable due to the superior analgesia of thoracic epidural techniques. Due to inflammation, surgery is technically more difficult in all infectious indications for pulmonary resection and there is a greater risk of massive hemorrhage which must be anticipated with appropriate venous access and preparations for transfusion.

Empyema

An empyema is a collection of pus between the visceral and parietal pleural layers often a complication of pneumonia or surgery. Empyema complicating lung resections occurs in

2–16% of cases and with a 40% increase in the associated perioperative mortality rate [21]. Mortality further increases when the empyema is associated with a BPF. The surgical interventions for patients with pleural empyema include: decortication (the method of choice when the underlying lung is unable to expand due to a thick inflammatory coat) or open window thoracostomy (the ideal method for drainage of the pleural cavity to control septic symptoms in patients with postpulmonary resection empyema) [22]. In less severe cases, tube drainage, antibiotic irrigation, and debridement may be sufficient.

Anesthetic Management

The major consideration in a patient with an empyema is that the patient might have an underlying BPF. In the absence of a history of a position-related productive cough, a BPF is extremely unlikely and there is a very low probability of contamination of healthy lung regions or of developing a tension pneumothorax from positive-pressure ventilation. However, if the history is unclear, it is safest to assume there may be a communication between the empyema and the bronchial tree and management should be based on the assumption of a BPF. Patients undergoing a decortication may have massive blood loss. If the lung has been chronically collapsed, expansion should be done gradually to avoid the development of pulmonary edema upon re-expansion. Extubation in the operating room is encouraged if the patient meets the standard criteria for extubation (see Chap. 2).

Lung Abscess

An abscess is a nonanatomic area of liquefactive necrosis of the lung often distal to an obstruction or following a pneumonia (see Fig. 33.4a, b). A patient with a lung abscess distal to an obstructing tumor may be relatively asymptomatic when they present for resection of their lung cancer. For this reason it is important that the anesthesiologist always examine the chest imaging preoperatively. All of the considerations for protection of healthy lung regions that apply to BPF and bronchiectasis also apply to the patient with a lung abscess. There is a significant risk of soiling the noninvolved lung when the abscess is manipulated during surgery. Anesthetic management principles are the same as for other underlying infectious indications for thoracic surgery (see Sect. “Bronchiectasis”).

Bullae

Bullae are thin walled air-filled intraparenchymal lung spaces caused by the loss of alveolar structural tissue (see Fig. 33.5). These are usually associated with emphysema but their exact cause is unclear. Although there is some confusion over terminology in this area, bullous-like lesions of the lung associated with congenital malformations or secondary to trauma or

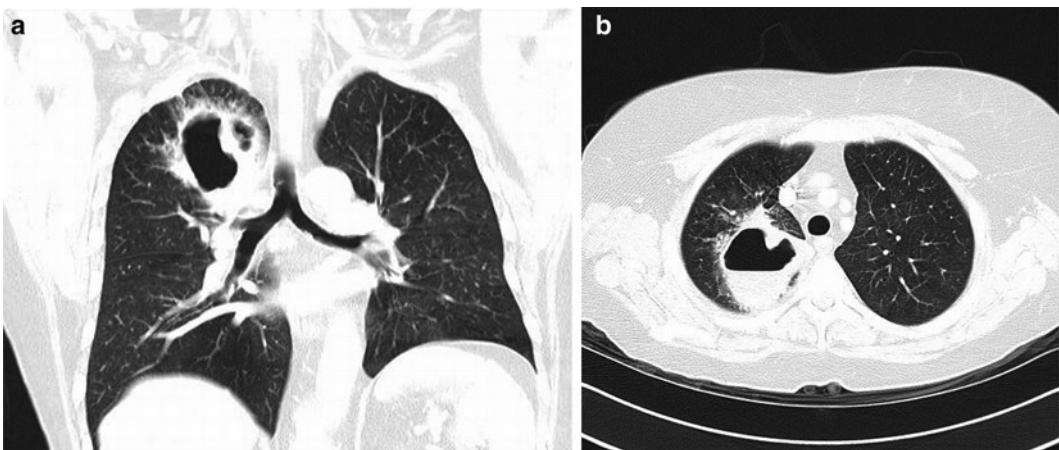


FIG. 33.4. Chest CT scans (a) coronal and (b) transverse of a patient with a right upper lobe lung abscess distal to an obstructing carcinoma. The typical thick walled appearance of the abscess can be appreciated. Since the CT scan is performed in the supine position the air-fluid level is only seen in the transverse plane. This patient had initially presented with a right upper lobe pneumonia 4 weeks previously. Following antibiotic treatment the patient had no symptoms related to the abscess at the time of admission for right upper lobectomy. These patients are at risk for soiling of uncontaminated lung regions during surgery from pus in the abscess. The optimal method of lung isolation is with a DLT.



FIG. 33.5. Preoperative chest X-ray of a patient with COPD and multiple bullae including a giant right upper lobe bulla for bullectomy. The bulla occupies nearly 50% of the right hemithorax.

infection are more correctly termed pneumatoceles or cysts [23]. There are no universally accepted surgical indications for resection of lung bullae. However, a patient with symptomatic dyspnea and a giant bulla (or bullae) which occupies $>30\%$ of a hemithorax and in whom X-ray and CT scans suggest that reasonably functional lung tissue can be restored to a more anatomically favorable position should be considered

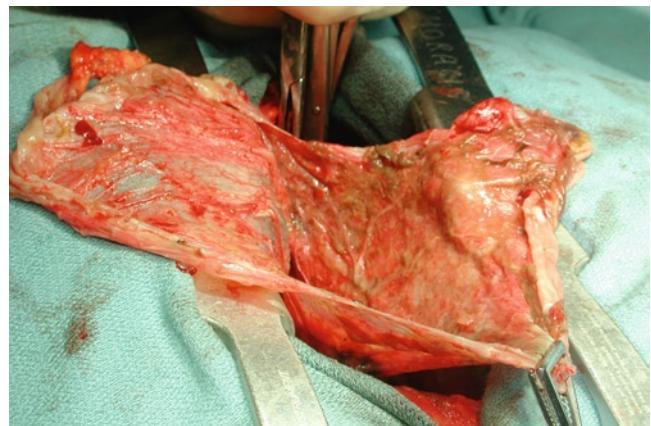


FIG. 33.6. A giant bulla exposed and opened during thoracotomy. The thin-walled structure of the bulla can be appreciated.

(see Figs. 33.6 and 33.7). Factors which support the effect of the bullae as a cause of a patient's dyspnea are a restrictive pattern on spirometry (proportional decrease of both FEV1 and FVC) and a discrepancy in lung volume studies in which the functional residual capacity (FRC) measured by plethysmography exceeds the FRC measured by helium dilution by >2 L [24].

The pathophysiology of bullae is complex. Ting described how the compliance pattern of bullae varied from that of surrounding lung tissue [25]. In the usual tidal volume range, bullae are more compliant than normal lung and fill preferentially during spontaneous ventilation. However, beyond the normal tidal volume range, bullae become much less compliant and the intrabulla pressure rises acutely as airway pressure increases. Much anesthesia literature has dwelt on the differences between communicating and noncommunicating bullae

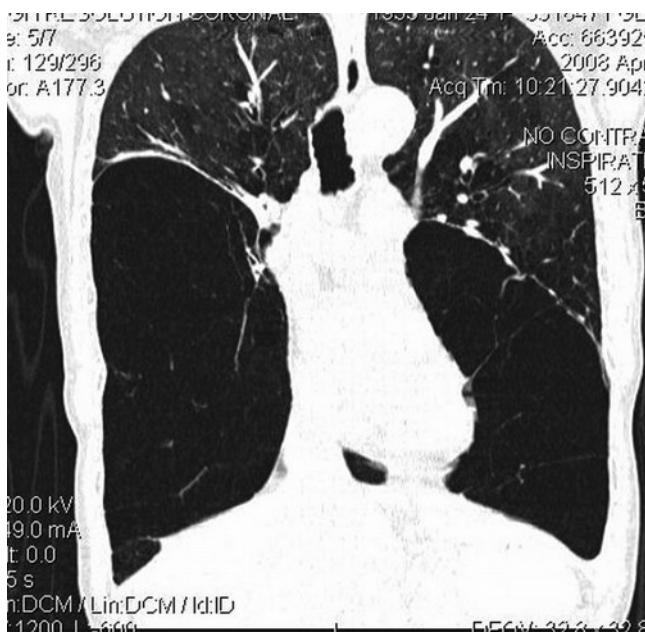


FIG. 33.7. Coronal CT scan of a patient with bilateral giant lower lobe bullae. During one-lung ventilation for bullectomy, the risk of contralateral bulla rupture and tension pneumothorax must always be kept in mind.

and the potential effects of a valve mechanism which could lead to hyperinflation and rupture of a bulla with positive pressure [26]. However, measurement of in vivo intrabullae pressures in patients using fine needles both before and during anesthesia has changed our understanding of the behavior of bullae. Morgan et al. [27] found no evidence of a valve mechanism. All bullae studied communicated with the central airways, although some very slowly. The typical compression pattern seen on X-ray or CT is more likely due to intralesional loss of structural alveolar support tissue with secondary elastic recoil of more normal lung regions (see Fig. 33.8a, b). Intrabulla pressure at FRC corresponds more with the mean airway pressure averaged over the respiratory cycle than with the peak airway pressure. Thus, during spontaneous ventilation, the intrabulla pressure will tend to be negative with respect to surrounding lung tissue. However, whenever positive pressure is used, the intrabulla pressure will rise in relation to surrounding lung regions. There is a risk of hyperinflation and rupture whenever positive pressure is used [28]. The complications of bulla rupture can be life threatening due to hemodynamic collapse from tension pneumothorax or inadequate ventilation due to a resultant BPF.

Relief of dyspnea symptoms and improved pulmonary function are well documented in series of patients after resection of giant bullae with most patients showing an increase in FEV1 of >0.3 L and excellent short-term improvement in quality of life, but with a decrease in improvement by 3 years [29]. Hypercapnia is not a contraindication to bullae resection. Lung infection must be meticulously treated preoperatively. Outcome depends on patient age, smoking history, and cardiac status.

In the postoperative period, lung air leaks are the major complication. The surgical approach can be by traditional or modified thoracotomy, sternotomy, or by VATS. Laser resection has been advocated to try and decrease the incidence of air leaks [30]. The advantages of laser in these operations versus reinforced automatic lung stapling devices remain to be proven. Various thoracoscopic and bronchoscopic procedures such as the subsegmental injections of fibrin glue have been used to deal with these air leaks [31].

The anesthetic considerations are similar to those for a patient with a BPF with the exceptions that it is best not to place a chest drain prophylactically as this may enter the bulla and create a fistula and there is not the risk of soiling healthy lung regions from extrapleural fluid that exists with a BPF. For induction of anesthesia it is usually optimal to maintain spontaneous ventilation until the lung or lobe with the bulla or bleb is isolated [32]. When there is a risk of aspiration or it is felt that the patient's gas exchange or hemodynamics may not permit spontaneous ventilation for induction, the anesthesiologist will have to use small tidal volumes with pressure-controlled ventilation and low airway pressures during positive pressure ventilation until the ipsilateral bronchus is isolated.

Blebs

A bleb is a subpleural collection of air under the visceral pleura caused by a ruptured alveolus [33]. The air dissects through the pulmonary parenchyma and enlarges to form a bubble on the surface of the lung. Blebs most commonly occur at the apices of the lung and can rupture into the inter-pleural space causing a pneumothorax. Patients are commonly tall individuals. A spontaneous pneumothorax presents with a spectrum of sudden-onset symptoms from mild to severe chest pain and dyspnea. Signs include decreased unilateral breath sounds on auscultation, hyperresonance on percussion, tachycardia, and possibly a pleural friction rub. ECG changes can occur due to rotational effects of the pneumothorax on the heart or due to decreased electrical conduction causing low voltage artifacts. Diagnosis is confirmed by chest imaging, a small pneumothorax can often be seen more easily on an expiratory film. Tension pneumothorax with hemodynamic compromise is usually related to positive pressure ventilation or chest trauma but is a possible complication of a spontaneous pneumothorax.

A single episode of spontaneous pneumothorax is usually treated conservatively with chest tube drainage until the air leak has stopped. Resection of blebs is commonly indicated for recurrent pneumothoraces, bilateral pneumothoraces, non-re-expansion of the lung, or prolonged chest tube drainage (>48 h). Resection of blebs after a single pneumothorax may be indicated if the patient's occupation exposes them to significant rapid fluctuations in atmospheric pressure (e.g., flight crews or scuba divers) or in patients with severe COPD. Resection is most commonly combined with a procedure to obliterate the pleural space by partial pleurectomy or pleural abrasion [34]. Resection of blebs is most often performed by

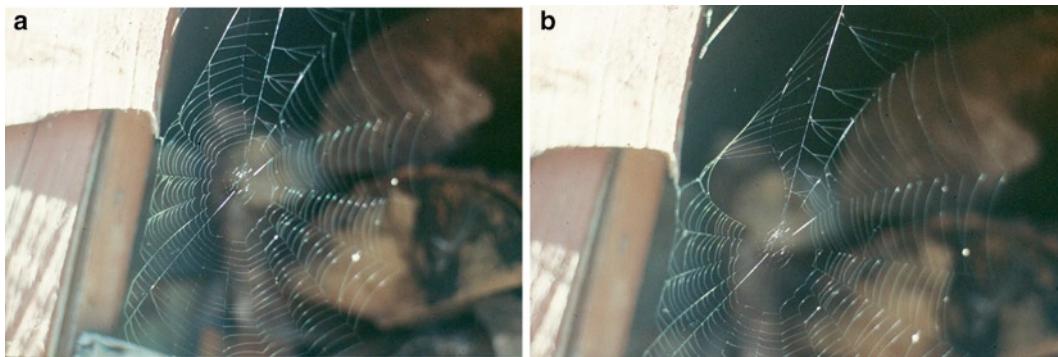


FIG. 33.8. (a) A spider's web seen on a woodbox on a sunny day used as a lung model to demonstrate the pathophysiology of bullae. (b) Breaking one septum of the spider's web causes a bulla to appear as elastic recoil pulls the web away from the area where structural support has been lost. Although the cells surrounding the bulla appear compressed, this is only due to redistribution of elastic forces. It is not positive pressure inside the bulla which causes this appearance of surrounding compression.

VATS. Although VATS procedures *per se* are generally associated with limited need for postoperative analgesia, pleurectomy or pleural abrasion is very painful.

Catamenial pneumothorax is a condition of recurrent pneumothoraces associated with menstruation. The exact etiology is unclear but may be related to endometrial implants on the visceral pleura or diaphragm or due to passage of air from the abdomen to the pleural space via congenital diaphragmatic defects. Surgical treatment is as for other conditions of recurring pneumothoraces but may also involve hormonal therapy [35].

A ruptured alveolus may dissect medially along peribronchial planes and present with a spontaneous pneumomediastinum. This is often associated with physical exertion and/or an increase in intrathoracic pressure. Symptoms include chest pain, and possibly cough, dyspnea, or dysphagia. Patients may have subcutaneous emphysema in the neck and chest wall. The differential diagnosis will include esophageal perforation and aortic dissection. Treatment is usually conservative unless pneumothorax develops [36].

Lung Cysts, Hydatid Cysts

Congenital bronchogenic cysts are products of abnormalities in the tracheobronchial budding process of lung organogenesis. They may occur peripherally within the lung parenchyma (70%) or centrally attached to the mediastinum or hilum (see Fig. 33.9) [37]. Bronchogenic cysts become problematic if they become enlarged, exerting a mass effect on functional lung or mediastinal structures “tension cyst,” if they rupture and create a pneumothorax, or if they become infected. Small cysts without communications to a bronchus are asymptomatic and may be incidentally noted as round clearly demarcated lesions on chest imaging. Communicating cysts often produce air-fluid levels, are prone to recurrent infection, and may trap air by a ball-valve mechanism risking rapid expansion or rupture. Infected cysts may be obscured by surrounding pneumonia or may be difficult to differentiate from an empyema. CT scans help differentiate cystic from solid lesions. Surgical excision



FIG. 33.9. Coronal MRI image of a patient with a congenital bronchial cyst (arrow) located just below the carina with minimal displacement and mild compression of the mainstem bronchi.

of bronchogenic cysts is generally recommended, whether or not a bronchial communication is evident.

Pulmonary Hydatid cysts are discussed under “Thoracic Anesthesia in Developing Countries”.

Pneumatocele

Pneumatoceles are thin walled, air-filled spaces generated by pulmonary infections or trauma. They usually appear in the first week of pneumonia and resolve spontaneously within 6 weeks. As with other lung cysts, potential complications of pneumatoceles include secondary infection, and enlargement as a result of air entrapment, with possible rupture or displacement

and compression of normal lung. Adverse hemodynamic consequences may result either from a tension pneumothorax or a tension pneumatocele. The latter is unusual and is presumed to result from a one-way valve mechanism, usually in the setting of positive pressure mechanical ventilation [38]. Occasionally surgical decompression is required, and has been performed by percutaneous needle aspiration, catheter drainage, or chest tube drainage under CT or fluoroscopic guidance. Rarely is thoracoscopic or open surgical drainage or excision required.

Pulmonary Arteriovenous Malformations

Direct communications between the pulmonary arteries and veins are uncommon lesions, most are congenital malformations (AVMs). The largest group of patients with pulmonary AVMs are those with hereditary hemorrhagic telangiectasia (HHT) (Osler–Weber–Rendu disease), an autosomal dominant vascular dysplasia (see Fig. 33.10). Patients with HHT usually have multiple pulmonary lesions and may also have telangiectasia of the skin or mucous membranes, recurrent epistaxis, or gastrointestinal bleeding. Pulmonary arteriovenous communications may also develop following trauma or infection and these are more correctly termed arteriovenous fistulae [39]. Patients may also develop pulmonary AV fistulae after Glenn shunts (a surgical anastomosis between the superior vena cava and the right pulmonary artery for complex congenital heart disease).

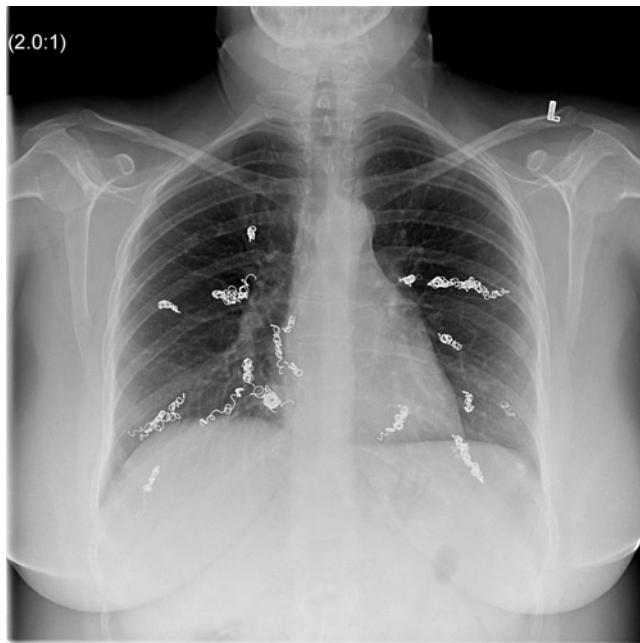


FIG. 33.10. Chest X-ray of a patient with hereditary hemorrhagic telangiectasia (HHT) who has been treated for recurrent episodes of hemoptysis. Multiple bilateral radiographic coils can be seen which have been placed in pulmonary AVMs.

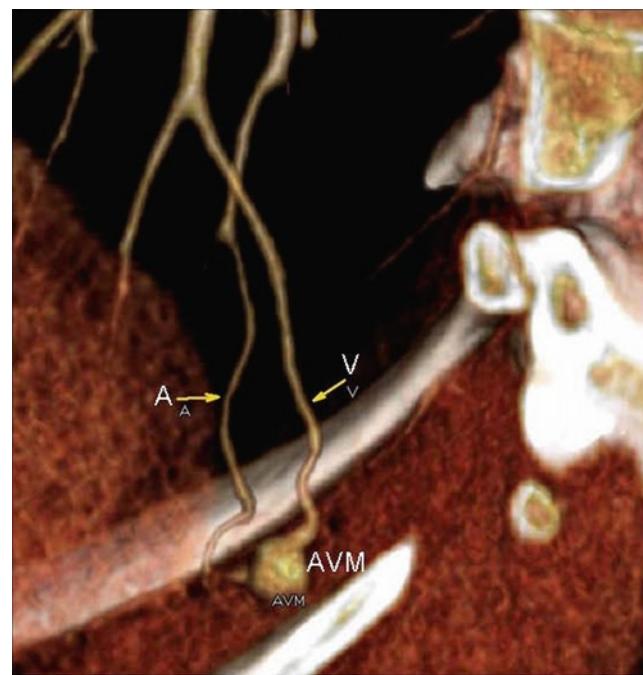


FIG. 33.11. CT angiogram of a single pulmonary AVM in the right lower lobe. A feeding pulmonary artery; V draining pulmonary vein. This AVM is suitable for treatment by radiologic coiling (photo courtesy of Dr. Elsie Nguyen, Department of Radiology, Toronto General Hospital).

Patients may present with exertional dyspnea, hemoptysis, or central cyanosis from right-to-left intrapulmonary shunting. Patients with AVMs are at high risk of developing neurological complications, either cerebrovascular accidents or transient ischemic attacks, so treatment is aggressive whenever possible. The diagnosis is confirmed by chest imaging techniques, primarily CT angiography (see Fig 33.11). Currently, the basis of treatment of pulmonary AVMs is by embolization in interventional radiology primarily by the endovascular placement of coils. Certain AVMs may not be suitable for embolization due to their anatomy (e.g., a large feeding vessel, central location) and surgery may be required (see Fig. 33.12a, b) [40].

Anesthetic Management

Several specific concerns must be remembered in the perioperative anesthetic management of patients with pulmonary AVMs (see Table 33.6). First these patients have right-to-left intrapulmonary shunting and the same concerns apply as for patients with congenital heart disease and right-to-left shunting. There is the risk of paradoxical systemic air emboli. All intravenous lines need to be meticulously de-aired and bubble filters should be used. The rate of induction with relatively insoluble volatile anesthetics will be delayed while the clinical onset of intravenous anesthetics will be accelerated. Second there is an increased risk of massive blood loss during

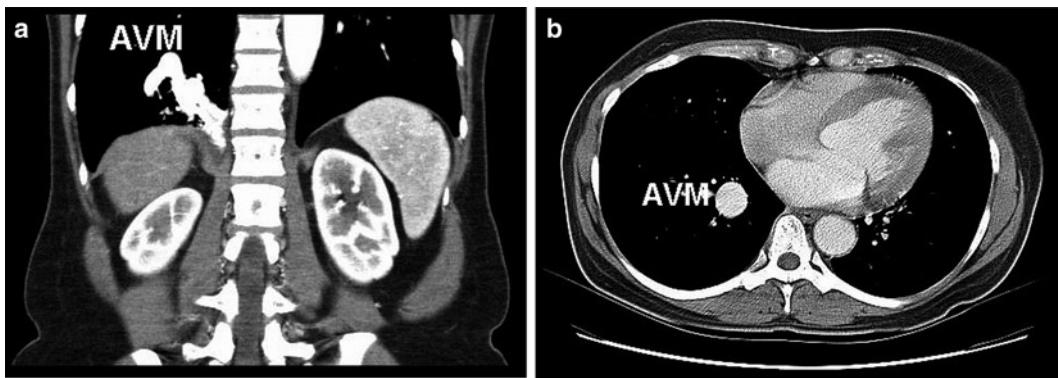


FIG. 33.12. Contrast chest CT scans, (a) coronal, (b) transverse plane, of a patient with a right lower lobe pulmonary AVM who required right lower lobectomy.

TABLE 33.6. Anesthetic considerations in a patient with a pulmonary arteriovenous malformation (AVM).

- Risk of systemic air emboli
- Delayed uptake of insoluble volatile anesthetics
- Increased speed of onset of intravenous anesthetics
- Risk of intraoperative airway hemorrhage
- Increased risk of massive blood loss during pulmonary resection
- Increased risk of desaturation during one-lung ventilation

surgical resection due to the increased vascularity. Third there is a risk of intraoperative airway hemorrhage when the lung is mobilized. Fourth there is an increased risk of desaturation during one lung ventilation due to the lack of response of the AVM to hypoxic pulmonary vasoconstriction. Mechanical techniques such as surgical compression of the ipsilateral pulmonary blood flow may be required to manage hypoxemia during one-lung ventilation. Placement of a Swan-Ganz catheter and inflation of the catheter balloon in the ipsilateral pulmonary artery has been used to improve oxygenation during thoracotomy for resection of a pulmonary AVM [41].

Decortication

Decortication is the surgical removal of the surface layer, membrane, or fibrous cover of the lung. It can be performed by thoracotomy or VATS depending on severity and nature of the problem. The procedure is usually performed when the lung is covered by a thick, inelastic pleural peel restricting lung expansion to restore the function of the lung and diaphragm and to obliterate the space in cases of recurring infections. It has best results when performed at the earliest possible opportunity. For chronic hemothoraces, decortication is indicated when there is 50% compression of the lung and there is no appreciable pulmonary expansion for 4–6 weeks following aspiration [42]. In pleural tuberculosis, therapy is primarily medical and surgery is only used for refractory pleural disease.

The primary concerns for anesthesia are intraoperative blood loss and air leaks. As for all inflammatory indications for intrathoracic surgery, there will be extensive vascularity of the surgical field with the potential for major intraoperative blood loss. Cross-matched blood and products and adequate invasive monitoring and vascular access, possibly including a central line, are indicated for open procedures. Lung isolation is indicated if there is a possibility of soiling of the nonoperative lung and may be required to maintain ventilation as there are frequently numerous air leaks from the raw surface of the operative lung. The possibility of surgical phrenic nerve injury should be kept in mind if the disease process involves the mediastinal pleura.

Thoracic Anesthesia in Developing Countries

Readers of this book are aware that thoracic anesthesia is a challenging specialty even in the best centers, with highly skilled professionals using the most sophisticated equipment and monitoring. The challenges are multiplied and magnified when the patients are poor, malnourished, anemic, and present late for treatment out of ignorance, superstition, or abject poverty. The spectrum of diseases is also quite different. There is a preponderance of infectious diseases such as those of pyogenic origin, tuberculosis, and helminthiasis. Medical personnel have limited training, inadequate equipment, and use antibiotics inappropriately or inadequately. Drugs, fluids, and safe blood are in short supply and there is often a fatalistic approach to all problems [43]. However, these conditions are not prevalent uniformly in all developing countries. Conditions or “degrees of development” vary both from country to country or within each country, so that at least in parts of a country the environment in which medicine is practiced is very similar to that practiced in the developed world. In most cases, maintaining the safety of the patient while treating them within the limits of our resources continues to be the challenge [44].

Anesthetic Management

Adequate preoperative preparation of “wet lungs” is crucial to the perioperative management and outcome. The aim should be to reduce the sputum production to the minimum possible. The patient should be managed with physiotherapy and dependent drainage, good hydration, frequent humidification/nebulization, and appropriate antibiotics and bronchodilators, as required. This regime should be started early and continued until surgery.

Except where a median sternotomy is required, as in the case of bilateral pulmonary hydatid cysts, most thoracotomies are performed in the lateral decubitus position. Isolation of the diseased or nondependent lung is required so as to prevent soiling of the “good” dependent lung, to provide adequate ventilation of the noninvolved lung as in the case of a BPF or to improve surgical exposure for intrathoracic procedures such as video-assisted thoracoscopy.

Isolation of the lung is often achieved with a disposable endobronchial DLT or bronchial blocker placed accurately with the help of a fiberoptic bronchoscope. However, an appropriate size fiberoptic bronchoscope, blocker, or DLT may not always be available. Reusable, autoclavable, red rubber Robertshaw or Carlen’s DLTs are most commonly used. Clinical judgment and experience are heavily relied upon for accuracy of placement. A commonly used blocker is a Fogarty arterial embolectomy catheter (Edwards Life Sciences, Irvine, CA, USA) placed on the diseased side through a rigid bronchoscope with an ETT passed alongside it subsequently. Its position is then confirmed clinically and with a fiberoptic bronchoscope, if available. Accidental dislodgement of a blocker can be catastrophic if there is an occlusion of the trachea or the mainstem bronchus of the dependent lung. The Arndt endobronchial blocker (Cook Medical, Bloomington, IN, USA) though very good is expensive and requires a fiberoptic scope for placement. The Univent tube (Fuji Systems Corporation, Tokyo, Japan) is expensive and though the smallest size has an internal diameter of 3.5 mm its outer

diameter is such that the smallest patient in whom it can be placed is 7–8 years old.

In places where DLTs are not available or in young children where the available DLTs are too large, many advocate the passage of a single-lumen ETT down the main bronchus of the dependent lung. The Murphy’s eye or a hole cut in the tube is expected to provide ventilation to the right upper lobe if the tube is down the right main bronchus. This method of lung isolation is neither complete nor effective and provides the anesthetist with a false sense of security. The tube may move during positioning or surgery and ventilation to the right upper lobe may be compromised. Furthermore, purulent secretions or blood will soil the dependent lung as the tube does not fit snugly in the main bronchus (see Fig. 33.13a). The tube is often smaller than that used for an ETT and suctioning is more difficult. Many of these problems can be overcome with the use of the largest possible ETT, a steep head down tilt, and frequent suctioning (see Fig. 33.13b). This technique is not possible with mechanical ventilation in the presence of a BPF but can be used with spontaneous ventilation [45] (see Fig. 33.14). Another option in case of a “wet lung” is for the surgeon to operate through an antero-lateral incision with the patient in the head down position. However, few surgeons are comfortable with this approach.

Tubes, monitors, and catheters should be secured and ventilation checked before positioning the patient and then checked again before the start of surgery. Monitoring is often only by a pulse oximeter, NIBP, a hand on the pulse and an eye on the surgical field. Ventilation is often manual but sophisticated monitors and ventilators are available in many centers. ECG, end-tidal CO_2 , temperature, intra-arterial blood pressure, and blood gas monitoring are used wherever possible.

Two working suctions, one for the surgeon and one for the anesthetist, are essential during thoracic anesthesia. If there is no central suction and electricity is unreliable, a foot operated pneumatic suction should be kept as a standby. Extra cylinders of oxygen and/or an oxygen concentrator should always be available.

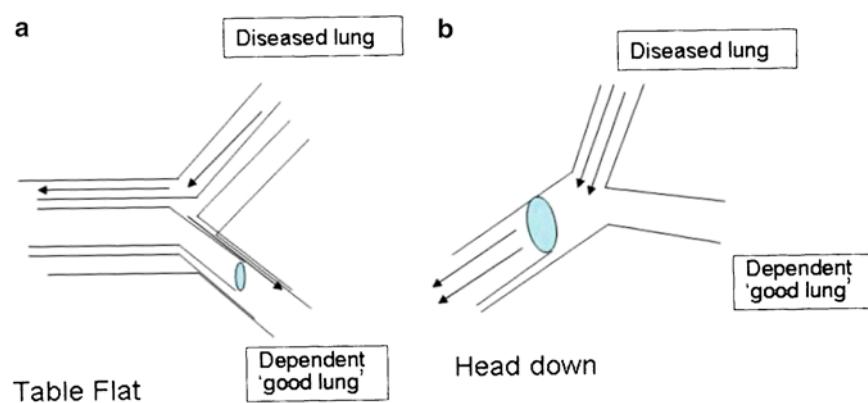


FIG. 33.13. Strategies to minimize soiling of the “good lung” using a single lumen ETT. Arrows show direction of flow of blood and secretions. (a) Shows a small ETT passed down the main bronchus of the dependent lung. It provides inadequate protection. (b) The use of a large ETT with the table tilted steep head down, though not foolproof, provides better protection and ease of suctioning.

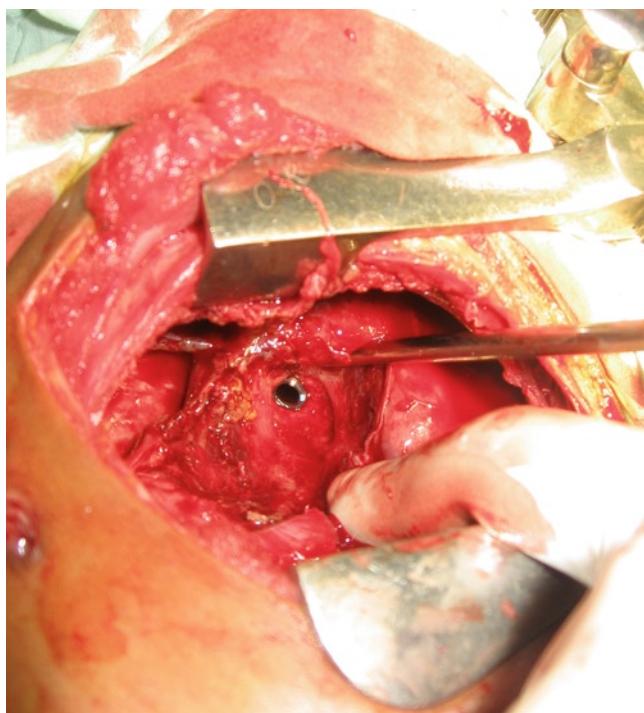


FIG. 33.14. A bronchoatmospheric fistula. The surgeon's view of the distal bronchial lumen of a left-sided DLT is seen through the open left upper lobe bronchus after evacuation of a lung abscess.

Tuberculosis

Tuberculosis (TB) is a major health hazard in developing countries. It is caused by the tubercle bacillus, *Mycobacterium tuberculosis*, which is usually transmitted by droplet infection. It affects the lungs most commonly but may affect any organ in the body. Diagnosis is by identification of the acid fast bacillus (AFB) in the sputum or gastric aspirate or by culture of the sputum or tissue (traditional cultures take 4–8 weeks, newer methods 2–4 weeks) [46].

Classically, primary tuberculosis appears as a small focus of exudative pneumonia in the periphery of the middle and lower zones of the lung. These drain into a hilar or paratracheal lymph node forming the “primary complex.” The primary site may also be in the pleura. In the majority of cases, these lesions heal spontaneously. In immunocompromised or malnourished patients, primary pulmonary tuberculosis may progress rapidly to clinical illness with pleural effusion, necrosis, and cavitation of the lung. Hematogenous spread from a caseating lymph node may affect any organ. Compression or erosion of bronchi may cause obstruction atelectasis [47].

Reactivation, post primary, “adult type,” or secondary tuberculosis results from endogenous reactivation of latent infection and almost always infects the apical or apical-posterior segment of an upper lobe where the relatively high oxygen tension favors mycobacterial growth. The tuberculous infiltration often increases in size with diffuse pneumonic consolidation.

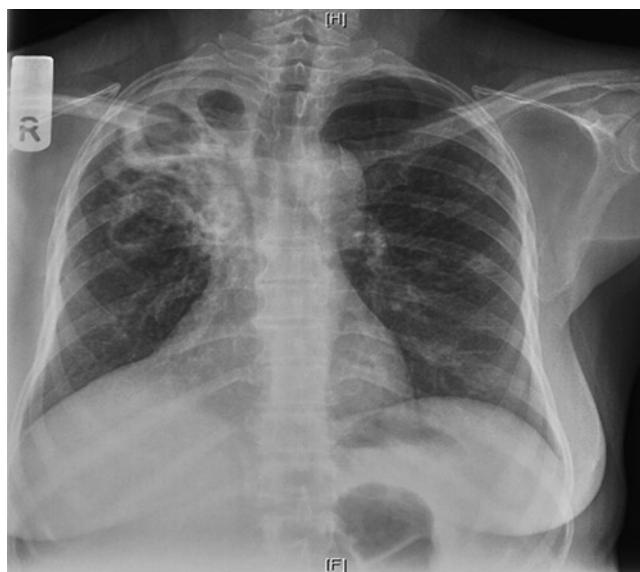


FIG. 33.15. The chest X-ray of a patient with pulmonary tuberculosis demonstrating fibrosis and cavitation of the right upper lobe with loss of lung parenchyma and distortion of the trachea.

It may undergo cavitation or invade the blood stream producing miliary tuberculosis. Productive cough with variable quantities of sputum and/or hemoptysis in a debilitated patient are hallmarks of pulmonary tuberculosis. Other pulmonary complications include pneumothorax, pleural effusion, empyema, BPF, massive hemoptysis, fibrosis with loss of parenchymal volume, and distortion of the tracheobronchial tree including bronchial stenosis (see Fig. 33.15).

In recent years, the convergence of human immunodeficiency virus (HIV) and the TB pandemic in developing countries has been a disaster practically unequaled in history with sub-Saharan Africa bearing the brunt of it. Infection with the tubercle bacillus proceeds rapidly to active disease and those coinfected with HIV are often smear negative. At present there is no sensitive, specific, rapid point of care diagnostic test for TB. The prolonged incubation time of traditional culture techniques delays time to diagnosis and institution of effective antituberculous therapy.

Anesthetic management principles are the same as for other infectious pulmonary diseases (see Sect. “Bronchiectasis”). Note that “open tuberculosis,” where bacilli are present in the sputum, is contagious and health care workers must take adequate precautions to protect themselves and other patients.

Hydatid Disease of the Lung or Pulmonary Echinococcus

Pulmonary hydatid cysts are watery, parasitic cysts, containing larvae of the dog tapeworm, *Echinococcus granulosus* [48]. Echinococcosis is worldwide in distribution and is endemic

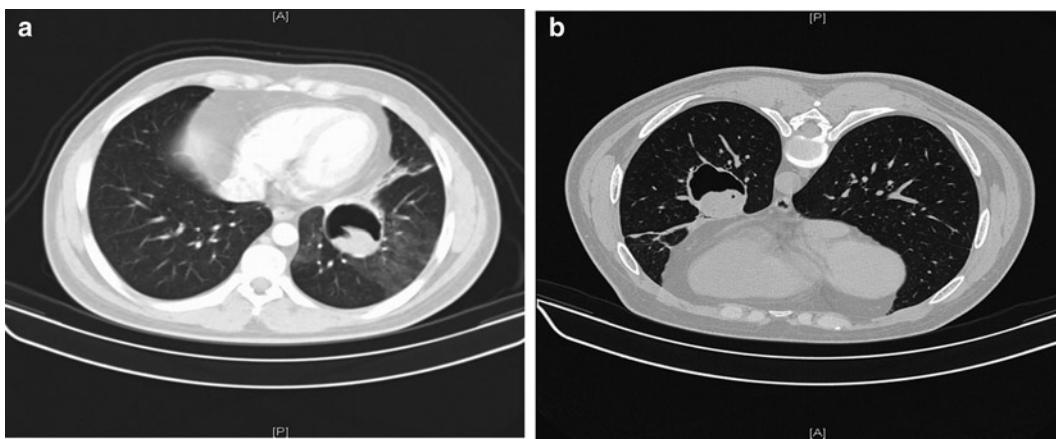


FIG. 33.16. Hydatid cyst mimicking a fungal ball in the left chest. (a) Supine and (b) prone CT images. Note that the contents of the cyst have moved with the position of the patient.

in Australia, New Zealand, South America, Arctic North America, Africa, and parts of Asia. Although primarily a problem in developing countries, patients may present for surgery in developed regions and the management goals are the same. The fully matured cysts are composed of three layers.

The outer layer, or pericyst, composed of inflamed fibrous tissue from the host; the exocyst, an acellular laminated membrane; and the innermost layer, or endocyst which is the germinative layer of the parasite producing brood capsules or secondary cysts that bud internally. An intact cyst, if large, may be filled with liters of fluid which is antigenic and contain debris consisting of hooklets and scolices referred to as "hydatid sand." Daughter cysts may develop directly from the endocyst resulting in multicystic structures. The disease occurs more in young individuals and the liver and lungs are the most commonly affected organs. Pulmonary hydatids may be unilateral (right lung in ~ 60%), 30% exhibit multiple pulmonary cysts, 20% are bilateral, and 60% are located in the lower lobes [49]. Pulmonary cysts increase in diameter at the rate of approximately 1–5 cm/year.

Clinical features depend on the site and size of the cysts. Small cysts remain asymptomatic for many years while large ones can become medically problematic in several ways. By mass effect, they may exert pressure on adjacent structures (bronchus, bone, great vessels, esophagus, etc.) causing bone pain, vascular and airflow obstruction, etc. Spontaneous or traumatic rupture may occur, sending fluid, parasites, or laminated debris into adjacent tissue, bronchus, pleura, or the circulation (systemic emboli). Hypersensitivity reactions can range from urticaria to life-threatening bronchospasm and anaphylaxis. Drainage into the bronchi may cause dramatic expulsion of fluid with respiratory distress or asphyxiation, depending on the amount of fluid involved. Rupture into the pleural space may result in a large hydro-pneumothorax, severe dyspnea, shock, suffocation, or anaphylaxis. Rupture becomes more dangerous and more likely as cysts become larger or the patient has been treated with helminthics (see below).

It is recommended that any cyst larger than 7 cm should be removed [50]. Ruptured cysts may become infected with bacteria or saprophytic or invasive fungi [51]. Hydatid disease is a rare cause of recurrent pulmonary embolism. Nonviable cysts show total calcification of their cyst walls. Diagnosis is by chest X-ray or CT scan (see Fig. 33.16a, b).

Surgical goals are complete removal of the intact unruptured cyst and maximal preservation of functional lung. Small, intact, peripheral cysts are often easily enucleated without loss of lung parenchyma. Enucleation involves blunt separation of the laminated layer from the surrounding pericystic zone (fibrous reactive host layer), with care to prevent rupture. Lung isolation or reduced airway pressure during dissection may be helpful in preventing early herniation of the cyst. Increased airway pressure at the time of delivery may aid delivery of the cyst (gentle hand ventilation with a sustained inspiratory "hold" is very helpful at this time). An alternative surgical strategy is to inject a scolicidal agent such as hypertonic saline, cetrimide, povidone iodine, formalin, ethanol, or hydrogen peroxide into the intact cyst to sterilize it, followed by aspiration of the contents and removal of the evacuated cyst. The operative field is protected with 1% formaldehyde or hypertonic saline.

Segmentectomy or lobectomy is indicated when single or multiple cysts occupy most of the segment or lobe. Patients with suppurative cysts should be prepared for surgery with postural drainage and antibiotics. The multiple bronchial openings in the residual cavity must be identified and closed. Multiple "leak tests" with saline in the residual opening may be required to locate all bronchial openings. Capitonage (i.e., quilting, or suturing of the anterior to posterior cyst walls) is recommended to close the cavity completely. A deliberately created bronchoatmospheric fistula (BAF) has been described in cases where there are large bronchial openings and there is fear of leaving a BPF or compromising air flow distally, if sutured. Ventilation is best managed spontaneously after creation of the BAF [52].

Medical management associated with surgery: It has been suggested that anthelmintics weaken the cyst wall increasing the likelihood of cyst rupture [53]. However, if spillage of cyst contents occurs either spontaneously or after manipulation either mebendazole or albendazole (better bioavailability) should be given to decrease the risk of secondary hydatidosis. If prophylactic medical therapy is chosen, it should start 4 days prior to surgery and be continued for 1–3 months.

Postoperative Care and Analgesia for Thoracic Patients

Most postoperative wards are understaffed and the care of the patient is often left to the relatives, be it feeding, cleaning, or physiotherapy. They provide not only nursing care but also love and support around the clock contributing immeasurably to the patients' recovery.

Postoperative pain relief is poorly addressed partly due to ignorance, the fear of respiratory depression, the nonavailability of drugs or equipment such as infusion pumps and inadequate nursing care. There is often no designated post-anesthetic care unit with trained personnel, monitoring, and equipment. The challenge lies in finding analgesic techniques that will provide pain relief without compromising respiration or require expensive equipment and trained personnel.

Ideally, postoperative pain relief must start preemptively. Acetaminophen or NSAIDS may be given with the premedication or suppositories placed after induction. An intercostal block or paravertebral block may be placed prior to incision and an interpleural catheter placed by the surgeon at the end of the procedure. Systemic narcotics may then be used sparingly intraoperatively and avoided postoperatively. This will ensure an awake, pain free patient who is breathing spontaneously at the end of surgery.

How does the interpleural block work? The local anesthetic, when placed in the paravertebral gutter, between the parietal and visceral pleura, diffuses through the parietal pleura and innermost intercostal muscles to block more than one intercostal nerve. It proceeds further medially to block the sympathetics as is seen by Horner's syndrome developing in high blocks especially if the patient is in a "head down" position. This block is unilateral and hypotension does not occur as it does in epidural blocks [54]. Interpleural blocks may be used in patients requiring analgesia for the T2 to T12 dermatomes. These blocks are especially useful in centers where there are no infusion pumps or close monitoring facilities. The interpleural catheters we use are 5 F or 7 F infant feeding tubes (inexpensive), placed by the surgeon, through a site other than the drain site, so as to ensure an airtight fit and prevent air entrainment. A three-way stopcock is fixed to the outer end of the catheter making top-ups cleaner and safer, with no air entrainment during top-ups. The "top-ups" of 0.25% bupivacaine, 0.5–0.75 mL/kg, are given four hourly after clamping the chest drain, with the patient lying lateral with the operated side up. The clamp on the chest drain is removed after 20 min.

This block is more effective in the child or adolescent than in the adult (perhaps the parietal pleura is thicker) or when an infusion is used (loss of drug through the chest drain). This regime is also not possible when there is a large air leak (clamping the tube could precipitate a pneumothorax) or if there is significant chest drainage (loss or dilution of drug). Complications, though rare, include pneumothorax, catheter displacement, and infection [55].

In centers where infusion pumps, monitors, and trained personnel are available, a thoracic epidural or patient-controlled analgesia (PCA) is used. Central neuraxial blocks require sterility and close hemodynamic monitoring.

Clinical Case Discussion

Case: A 65-year-old female patient has a right pneumonectomy for lung cancer. The patient is an ex-smoker with no significant comorbidities. After placement of a thoracic epidural catheter and induction of general anesthesia, the patient's airway is managed with a 37 F left-sided DLT. After an uncomplicated 3-h operation, the patient is extubated in the operating room and transferred in stable condition to the recovery room. The right chest drain is removed on postoperative day 1 on the surgical ward (see Fig. 33.17a). The patient's postoperative course is uncomplicated for the first 6 days. On day 7 the patient suddenly develops a cough productive of large amounts of sero-sanguinous fluid and becomes acutely dyspneic, hypoxemic, tachycardic, and hypertensive.

- What is the most likely diagnosis?
- What is the differential diagnosis?
- How do you confirm the diagnosis?
- What is the correct treatment?

Diagnosis: In the clinical context of the sudden onset of dyspnea in the early postoperative period following a pneumonectomy with the new onset of a productive cough, the most likely diagnosis is a BPF due to the dehiscence of the bronchial stump. The differential diagnosis would include a pulmonary embolus, pneumonia, myocardial infarction, cardiac herniation, and postpneumonectomy pulmonary edema. The diagnosis is confirmed by the chest X-ray (see Fig. 33.17b) which shows the new appearance of multiple air-fluid levels in the right hemithorax, which is pathognomonic for a post-operative BPF. When this occurs in the early postoperative period following a pneumonectomy associated with severe respiratory compromise it requires immediate surgical repair of the fistula.

Management: The patient is transferred to the operating room for an emergency right thoracotomy and repair of BPF.

- What are the specific anesthetic considerations for repair of a BPF?
- Prior to induction of anesthesia what procedure must be performed for this patient?
- What are the options for induction of anesthesia with a BPF?

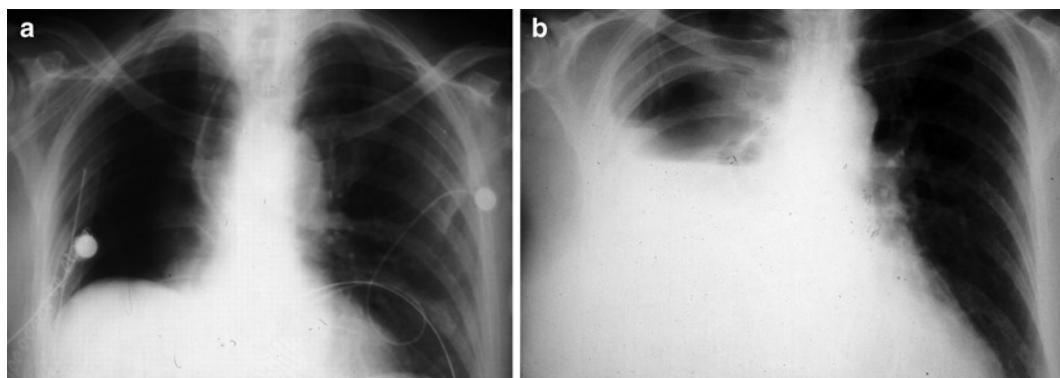


FIG. 33.17. (a) Postoperative chest X-ray of a 65-year-old patient day 1 following a right pneumonectomy. (b) The same patient on postoperative day 7. The fluid volume in the right hemithorax has decreased from the previous day (day 6, not shown) and there are new multiple air-fluid levels.

- What are the options for airway management for this patient?
- Which of these options is the most appropriate management for this patient?

Discussion: The specific anesthetic concerns in a patient with an early postoperative BPF are avoidance of soiling of the healthy lung by infected secretions from the operative hemithorax and avoidance of tension pneumothorax and ensuring adequate gas exchange by minimizing loss of expired tidal volume via the fistula (see Sect. “Bronchopleural Fistula”). This patient should have a chest drain placed in the right hemithorax prior to induction of anesthesia to avoid the possibility of tension pneumothorax with positive pressure ventilation and to drain as much of the infected fluid as possible from the right chest. Options for induction of general anesthesia in a patient with a BPF are awake fiberoptic intubation and lung isolation prior to induction of anesthesia, induction of anesthesia maintaining spontaneous ventilation until lung isolation is confirmed, or modified rapid sequence induction avoiding positive pressure ventilation until lung isolation is achieved. The options for airway management in this case are either a single- or double-lumen left-sided endobronchial tube, a bronchial blocker is not an option due to the short length of the postpneumonectomy bronchial stump. In this elderly patient with dyspnea and hypoxemia, the optimal management would be a modified rapid sequence induction with direct FOB guidance of either a single- or DLT into the left mainstem bronchus. The patient should be in a slight head up and slight right-lateral tilt position during induction to decrease the risk of soiling of the left lung.

References

1. Cerfolio RJ. Advances in thoracotomy tube management. *Surg Clin North Am.* 2002;82:833–48.
2. Singh N, Agarwal R. Bronchopleural fistula or alveolopleural fistula? *Chest.* 2006;130:1948.
3. Marshall MB, Deeb ME, Bleier JI, et al. Suction vs. underwater seal after pulmonary resection: a randomized controlled study. *Chest.* 2002;121:831–5.
4. Wright CD, Wain JC, Mathisen DJ, et al. Postpneumonectomy bronchopleural fistula after sutured bronchial closure: incidence, risk factors, and management. *J Thorac Cardiovasc Surg.* 1996;112:1367–72.
5. Nagahiro I, Aoe M, Sano Y, et al. Bronchopleural fistula after lobectomy for lung cancer. *Asian Cardiovasc Thorac Ann.* 2007;15:45–8.
6. Pomerantz AH, Derasari MD, Sethi SS, Khan S. Early post-pneumonectomy bronchial stump fistula. *Chest.* 1988;93:654–7.
7. Zaheer S, Allen MS, Cassivi SD, et al. Postpneumonectomy empyema: results after the Clagett procedure. *Ann Thorac Surg.* 2006;82:279–84.
8. Mulot A, Sepulveda S, Haberer JP, et al. Diagnosis of postpneumonectomy bronchopleural fistula using inhalation of oxygen or nitrous oxide. *Anesth Analg.* 2002;95:1122–5.
9. West D, Togo A, Kirk A. Are bronchoscopic approaches to post-pneumonectomy bronchopleural fistula an effective alternative to repeat thoracotomy? *Interact Cardiovasc Thorac Surg.* 2007;6:547–50.
10. Patane PS, Snell BA, Mahla ME. Awake fiberoptic endobronchial intubation. *J Cardiothorac Anesth.* 1990;4:229–31.
11. Karzai W, Klein U. Lobectomy for cavitating lung abscess. *Br J Anaesth.* 2001;86:735–6.
12. Bailey KM, Gottleib EA, Edmonds JL, et al. Anesthetic management of a young adult with complex congenital heart disease and a bronchopleural fistula. *Anesth Analg.* 2006;103:1432–5.
13. Williams A, Kay J. Thoracic epidural anesthesia for thoracoscopy, rib resection, and thoracotomy in a patient with a bronchopleural fistula postpneumonectomy. *Anesthesiology.* 2000;92:1482–5.
14. Tietjen CS, Simon BA, Helfaer MA. Permissive hypercapnia with high-frequency oscillatory ventilation and one-lung isolation for intraoperative management of lung resection in a patient with multiple bronchopleural fistulae. *J Clin Anesth.* 1997;9:69–73.
15. Poulin V, Vaillancourt R, Somma J, et al. High frequency ventilation combined with spontaneous breathing during bronchopleural fistula repair. *Can J Anesth.* 2009;56:52–6.

16. Baumann MH, Sahn SA. Medical management and therapy of bronchopleural fistulas in the mechanically ventilated patient. *Chest*. 1990;97:721–8.
17. Ost D, Corbridge T. Independent lung ventilation. *Clin Chest Med*. 1996;17:591–601.
18. Otruba Z, Oxorn D. Lobar bronchial blockade in bronchopleural fistula. *Can J Anaesth*. 1992;39:176–8.
19. Cowan MJ, Gladwin MT, Shelhamer JH. Disorders of ciliary motility. *Am J Med Sci*. 2001;321:3–10.
20. Laros CD, Van denBosch JMM, Westermann CJ, et al. Resection of more than 10 lung segments. *J Thorac Cardiovasc Surg*. 1988;95:119–23.
21. Pairolo PC, Deschamps C, Allen MS, et al. Postoperative empyema. *Chest Surg Clin North Am*. 1992;2:813–20.
22. Chan DT, Sihoe AD, Chan S, et al. Surgical treatment for empyema thoracis: is video-assisted thoracic surgery “Better” than thoracotomy? *Ann Thorac Surg*. 2007;84:225–31.
23. Klingman RR, Angelillo VA, DeMeester T. Cystic and bullous lung disease. *Ann Thorac Surg*. 1991;52:576–84.
24. Takashi I, Natanabe Y, Fukutami G. Simultaneous bilateral operations for bullous emphysema by median sternotomy. *J Thorac Cardiac Surg*. 1981;81:732–8.
25. Ting EY, Klapstock R, Lyons HA. Mechanical properties of pulmonary cysts and bullae. *Am Rev Respir Dis*. 1963;87:538–47.
26. Caseby NG. Anesthesia for the patient with coincidental giant lung bullae. *Can Anaesth Soc J*. 1981;28:272–9.
27. Morgan MDL, Edwards CW, Morris J, Matthews HR. Origins and behaviour of emphysematous bullae. *Thorax*. 1989;44:533–40.
28. Cohen E, Kischner PA, Benumof JL. Case conference 1–1990, bilateral bullectomy. *J Cardio Thorac Anesth*. 1990;4:119–26.
29. Schipper PH, Meyers BF, Battafarano RJ, et al. Outcomes after resection of giant emphysematous bullae. *Ann Thorac Surg*. 2004;78:976–84.
30. Wakabayashi A. Thoracoscopic laser pneumoplasty in the treatment of diffuse bullous emphysema. *Ann Thorac Surg*. 1995;60:936–42.
31. Oizumi H, Hoslin E, Aoyoma K, et al. Surgery of giant bullae with tube drainage and bronchofiberoptic bronchial occlusion. *Ann Thorac Surg*. 1990;49:824–9.
32. Eagle C, Tang T. Anesthetic management of a patient with a descending thoracic aortic aneurysm and severe bilateral bullous pulmonary disease. *Can J Anaesth*. 1995;42:168–72.
33. Beauchamp G, Oulette D. Spontaneous pneumothorax and pneumomediastinum. In: Pearson FG, editor. *Thoracic surgery*. 2nd ed. Philadelphia: Churchill Livingston. 2002;1195.
34. Schramel F, Postmus PE, Vanderschueren RG. Current aspects of spontaneous pneumothorax. *Eur Respir J*. 1997;10:1372–8.
35. Alifano M, Trisolini R, Cancellieri A, et al. Thoracic endometriosis: current knowledge. *Ann Thorac Surg*. 2006;81:761–9.
36. Kwon JS, Blum MG, Kalhan R. A 23-year-old woman with sudden-onset dyspnea and chest pain penetrating to the back. *Chest*. 2008;133:574–8.
37. Reynolds M. Congenital lesions of the lung, Chapter 79. In: Shields TW, LoCicero J, Ponn RB, editors. *General thoracic surgery*. 5th ed. Philadelphia: Lippincott Williams and Wilkins. 2000;937.
38. Shen H, Lu FL, Wu H, et al. Management of tension pneumatocele with high-frequency oscillatory ventilation. *Chest*. 2002;121:284–7.
39. Coley SC, Jackson JE. Pulmonary arteriovenous malformations. *Clin Radiol*. 1998;53:396–404.
40. Georgiou GP, Berman M, Vidne BA, et al. Pulmonary arteriovenous malformation treated by lobectomy. *Eur J Cardio Thorac Surg*. 2003;24:328–30.
41. Abiad MG, Cohen E, Krellenstein DJ, et al. Anesthetic management for resection of a giant pulmonary arteriovenous malformation. *J Cardiothorac Vasc Anesth*. 1995;9:89–94.
42. Rocco G, Descamps C, Deslariers J. Fibrothorax and decortication. In: Patterson GA, editor. *Pearson’s thoracic and esophageal surgery*. 3rd ed. Philadelphia: Churchill Livingston. 2008;1170–85.
43. Jacob R. Anesthesia for thoracic surgery in children in developing countries. *Paediatr Anesth*. 2009;19:19–22.
44. Jacob R. Challenges in the practice of thoracic anaesthesia in developing countries. In: Slinger P, editor. *Progress in thoracic anesthesia*. Baltimore: Lippincott Williams and Wilkins. 2004;267–85. p. 267–85.
45. Kaliaperumal I, Jacob R, Lionel KR, Chacko J. An unusual presentation of bronchopleural fistula. *Pediatr Anesth*. 2008;18:1268–9.
46. Ravaglione RJ, O’Brien RJ. Tuberculosis. In: Fauci AS, Braunwald E, Kasper DL, Longo DL, Jameson JL, Loscalzo J, editors. *Harrison’s principles of internal medicine*. 17th ed. McGraw Hill: New York. 2008;1006–20.
47. Mendelson M. Diagnosing tuberculosis in HIV infected patients: challenges and future prospects. *Br Med Bull*. 2007;1–17. doi:10.1093/bmb/ldm009.
48. Morar R, Feldman C. Pulmonary echinococcus. *Eur Respir J*. 2003;21:1069–77.
49. Thumler J, Munoz A. Pulmonary and hepatic echinococcus in children. *Pediatr Radiol*. 1978;7:164–71.
50. Aletras H, Symbas PN. Hydatid disease of the lung. In: Shields TW, LoCicero J, Ponn RB, editors. *General thoracic surgery*. 5th ed. Philadelphia: Lippincott Williams and Wilkins. 2000;1113.
51. Date A, Zachariah N. Saprophytic mycosis with pulmonary echinococcosis. *J Trop Med Hyg*. 1995;98:404–6.
52. Jacob R, Sen S. The anesthetic management of a deliberately created bronchoatmospheric fistula in bilateral pulmonary hydatids. *Paediatr Anaesth*. 2001;11:733–6.
53. Kuzucu A, Soysal O, Ozgel M, Yologlu S. Complicated hydatid cysts of the lung: clinical and therapeutic issues. *Ann Thorac Surg*. 2004;77:1200–4.
54. Jacob R, Soundravalli B. Analgesic effect of interpleural bupivacaine after thoracic and upper abdominal surgery. *Indian J Anaesth*. 1994;42:321–8.
55. Stromskag KE, Minor B, Steen PA. Side effects and complications related to interpleural analgesia: an update. *Acta Anaesthesiol Scand*. 1990;34:473–7.

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Key Points

- With massive hemoptysis, death is usually caused by asphyxiation rather than by exsanguination.
- Urgent management focuses on the prevention of asphyxia while the source of bleeding is addressed.
- Endobronchial and/or angiographic control is usually possible.
- Bronchial artery embolization is now the treatment of choice.
- There is now less indication for surgery and surgical results are better in stabilized, “elective,” nonbleeding patient.
- Pulmonary artery injury is rare but has high mortality.

Introduction

Massive hemoptysis is a medical emergency that places the patient at risk of asphyxiation and death. Because of the explosive clinical presentation of massive hemoptysis, it is essential to respond quickly and appropriately. This is a potential lethal condition that deserves to be investigated thoroughly and brought under control promptly [1].

The definition of massive hemoptysis may vary depending on the publication. It is usually based on the volume

of blood expectorated. In the literature, we can find large variations between the definitions. They range from 100 to 1,000 mL/24 h [2–4]. By consensus (see Table 34.1), massive hemoptysis is defined as a rate of bleeding exceeding 600 mL/24 h, meaning 25 mL/h. Only 1.5–5% of hemoptysis are really massive [1]. Exsanguinating hemoptysis is defined as a bleeding rate exceeding 150 mL/h or blood loss over 1,000 mL/24 h or over 300 mL during one expectoration [5]. Quantification of massive hemoptysis may be difficult and, from a clinical point of view, such criteria are not useful. Based on the fact that the anatomic dead space of the major tracheobronchial tree is about 200 mL in most adults [6], other definitions relying on the magnitude of the clinical effects have been proposed. Massive hemoptysis can be defined as the volume of expectorated blood that is life-threatening mainly by virtue of airway obstruction and rarely by blood loss.

Massive hemoptysis compared to moderate or minor hemoptysis represents a higher risk of mortality for the patient. Published series on patients presenting massive hemoptysis showed a mortality rate with medical management varying from 12 to 50%. Mortality rate was greater than 50% in patients not treated adequately [1]. Decision-making is a multidisciplinary process involving a critical care physician, pulmonary medicine bronchoscopist, interventional radiologist, thoracic surgeon, and anesthesiologist.

TABLE 34.1. Definition of hemoptysis.

Hemoptysis	Massive	Exsanguinating
One expectoration (mL)		>300
mL by hour	>25	>150
mL by 24 h	>600	>1,000

Historical Considerations

Massive hemoptysis treatment was at first exclusively surgical. From the 1940s to the 1960s, different surgical approaches have been used to control and treat massive hemoptysis. In 1973, Remy et al. [7] changed management forever with the first report of bronchial artery embolization (BAE). Hiebert in 1974 [8], described the first successful use of a Fogarty balloon catheter through a rigid bronchoscope to tamponade bleeding in a moribund patient with massive bronchial hemorrhage. Subsequently, the use of the bronchoscope progressively changed from a rigid device to the flexible fiberoptic bronchoscopy (FOB). More recently, the role of early bronchoscopy, mainly with a FOB, is questioned since BAE is easy to perform and so effective.

Since the introduction of radiological embolization, there are less frequent interventions by anesthesiologists for massive hemoptysis. With the rapid use of BAE, potentially massive hemoptysis are rapidly controlled and there is less and less need for surgical interventions (emergent, semi-emergent, or elective posttreatment), and therefore there is less anesthesia. Consequently, an anesthesiologist is only occasionally required to help with airway management, for lung protection and for assistance during radiological intervention.

The literature usually refers to old publications and there are only retrospective series or anecdotal reports that support recommendations for investigation and a treatment plan for massive hemoptysis. It is easy to understand that it is very difficult to design a prospective, randomized, controlled trial in this type of population.

Etiologies

Hemoptysis is defined by coughing of blood that originates from the tracheo-bronchial tree or pulmonary parenchyma. There are many potential causes of massive hemoptysis. It is very important to rapidly rule out any nonpulmonary bleeding since it can be originating from the nasopharynx or from the upper gastrointestinal tract.

The lungs have a dual blood supply, the bronchial arteries and branches from the aorta that brings nutrients to the lung parenchyma and major airways. The bronchial tree is implicated in massive hemoptysis in more than 90% of cases. Bronchial arteries typically arise from the thoracic aorta or its branches, although as many as 30% can arise from other locations [6]. The same vessels that supply the bronchial arteries

TABLE 34.2. Possible causes of massive hemoptysis.

Infectious
Bronchiectasis (including cystic fibrosis)
Chronic bronchitis
Tuberculosis
Nontuberculous mycobacteria
Lung abscess
Necrotizing pneumonia
Mycetoma
Cardiovascular
Arterio-venous malformation
Pulmonary embolism or infarct
Mitral stenosis
Aortic aneurysm or broncho-vascular fistula
Vasculitis, Wegener's granulomatosis
Neoplastic
Lung cancer
Bronchial adenoma
Pulmonary metastases
Miscellaneous
Aspirated foreign body
Pulmonary contusion, trauma
Idiopathic pulmonary hemosiderosis
Iatrogenic: trans-thoracic or trans-bronchial biopsy, or pulmonary artery catheter

may also supply the esophagus, the mediastinal nodes, and, more importantly, the spinal cord, through a complex anastomotic network [9]. Bronchial arteries are a high-pressure system and bronchial arterial bleeding is distinctively brisk and bright red.

Pulmonary arterial circulation is responsible for gas exchange; it is involved in less than 5–10% of cases as origin of massive hemoptysis. The pulmonary bed is a high-compliance and usually a low-pressure system (15–20 mmHg systolic and 5–10 mmHg diastolic). If there is pulmonary artery hypertension, this low-pressure system may be modified to a high-pressure system, reaching sometimes the systemic level. Dark blood is more consistent with pulmonary artery bleeding since the blood is not sufficiently oxygenated.

Hemoptysis originates from systemic, namely bronchial, or from pulmonary vessels. The most frequent causes of bronchial tree hemoptysis are inflammatory lung disease (bronchiectasis and tuberculosis) and neoplasm (see Table 34.2). The most common causes of hemoptysis from the pulmonary circulation are arterio-venous malformation (AVM) and Rasmussen's aneurysms (due to tuberculosis). Pulmonary artery iatrogenic rupture from a pulmonary catheter (Swan-Ganz) happens rarely, but as anesthesiologists are frequently implicated in its origin, we will discuss it in depth later in this chapter.

Clinical Manifestation

In the acute phase of hemoptysis, there is an accumulation of blood in the dependant part of the lungs. Through the cough reflex, blood is expelled, producing the hemoptysis.

During that time, blood may disperse bilaterally in the bronchial tree and the diagnosis of the side of bleeding may be confusing.

The degree of bleeding may be easily underrated because the volume of blood contained in the involved lobes or lungs is not evident and may be significant [1]. Many patients with hemoptysis have compromised lung function, and even small quantities of blood in the bronchial tree can lead to significant respiratory distress. Expectorated blood is often swallowed and cannot be measured. Asphyxia is the most life-threatening manifestation of massive hemoptysis, well before hemodynamic instability appears. Asphyxia is the usual cause of death associated with massive hemoptysis.

Initial Management of Massive Hemoptysis

There is little consensus regarding the optimal management of patients presenting with massive hemoptysis. Moreover, there are few recent, post2000, large series of patients studied. In this section, we will present conclusions of these studies, some consensus from the literature and also various controversies.

Initial management of massive hemoptysis needs to achieve a number of objectives quickly and simultaneously. The initial step in management of hemoptysis is to differentiate between minor and massive hemoptysis. The approach to the patient presenting massive hemoptysis can be generally done in three steps: [10] airway protection, localization, and treatment. The initial approach to the patient should be dictated by the clinical presentation. Patients with rapid bleeding or severe functional decompensation need firstly protection of the airway, meaning that every effort should be made to protect the nonaffected lung against blood spillage and to maintain adequate gas exchange to prevent asphyxia [11]. Hypoxia secondary to lung spillage or blood clots is the main cause leading to death. Secondly, it is essential to localize the source of bleeding, meaning finding the site (and etiology...), or at least the side of the massive hemoptysis. Thirdly, the administration of the specific therapy is mandatory. Treatment options include conservative medical therapy, endobronchial therapy, arterial embolization, or surgery.

All patients presenting massive hemoptysis should be admitted to an intensive care unit for further investigation and treatment or transferred to the radiological suite for computed tomographic (CT) or angiogram, or less frequently, to the operating room. While undergoing diagnostic procedures, the patient should be kept as upright as possible and 100% oxygen should be administered. Appropriate venous access should be put in place and blood should be available from the blood bank. A coagulation profile should be prepared to demonstrate any coagulopathy, including platelet dysfunction from drugs such as acetylsalicylic acid (Aspirin®) or clopidogrel (Plavix®). Every effort should be made to reverse anticoagulation, if possible. Invasive therapeutic measures are not indicated for the control of hemoptysis caused by anticoagulant therapy,

blood dyscrasia, or Goodpasture's syndrome [1]. Blood loss from these causes is rarely massive enough to significantly affect hemodynamics, slight hypotension may be treated with volume replacement.

Light sedation with anxiolytic drugs or cough suppression drugs are rarely useful in the acute phase of massive hemoptysis [11]. Once the immediate danger has passed and bleeding is settling, these drugs may be used to depress the excessive or violent coughing that can aggravate or stimulate hemoptysis [6]. Do not administer bronchodilators because they can have vaso-dilator results and may precipitate renewed bleeding [12].

Life-Threatening Intervention

Faced with massive hemoptysis, several strategies to prevent airway contamination should be available. If lung isolation is delayed or not used, the patient intubated or not, should be placed in the lateral decubitus position with the bleeding lung on the dependant (inferior) side to prevent spillage to the unaffected lung (nondependant, superior side).

Lung isolation may be used to avoid spillage to the unaffected lung by blood from the bleeding lung. Lung isolation can be performed with different techniques including a selective endobronchial intubation with a standard endotracheal tube, or the use of a bronchial blocker (BB) or insertion of a double-lumen tube (DLT). The two last lung isolation techniques are not specific to hemoptysis as they are used regularly during anesthesia for thoracic surgery [13] (see Chap. 16).

Mainstem bronchial selective intubation with a large uncut endotracheal tube is facilitated by the use of a fiberoptic bronchoscope (FOB), if the visualization is good enough to permit the guidance of the tube. Blood and clots may obstruct the view from FOB. Blood highly absorbs the light of the FOB, and consequently alters its capacity to identify the tracheal bifurcation and the guidance of the endobronchial tube. Blind endobronchial insertion may be attempted and verified by auscultation. The presence of large amount of blood in the main airway may hinder auscultation.

BBs may be used for lung isolation or act as a therapeutic avenue when facing massive hemoptysis. Bronchial blocking devices may be used for lung separation when a DLT is not immediately available or when there is some difficulty in inserting a DLT (e.g., percutaneous tracheotomy [14]). As for any other lung isolation devices, the use of FOB is mandatory, but the airway visualization may be difficult because of the presence blood and clots. A BB may be used in a non-intubated (through nostrils) or intubated patient. It can be positioned and stabilized alongside or inside the lumen of the endotracheal tube or DLT. In some situations, the BB may be introduced through a DLT. At that time, the use of very small FOB (2.8 mm) may be necessary, mainly with a smaller size DLT (35–37 Fr).

Nevertheless, endobronchial blockers may be used when facing a catastrophic exsanguinating hemoptysis [15],

as a temporary measure in life-threatening situations until a more specific treatment is applied. It is an excellent method to achieve control of the bleeding and to protect the contralateral lung and potentially the ipsi-lateral nonbleeding lobes or segments. The technique of endobronchial tamponade for bleeding control in massive hemoptysis was first introduced by Hiebert in 1974 [8]. The author occluded a bleeding bronchus with a balloon catheter inserted through a rigid bronchoscope. Different catheters have been used for this application: Foley catheter, Fogarty catheter [16], Swan-Ganz catheter, specific double balloon catheter, and more recently BBs. In addition to the tamponade effect, the administration of vasoactive drugs is possible through the inner channel [16]. This gives time to proceed with a therapeutic and more definitive intervention. The BB should be replaced by a DLT or a single-lumen tube to permit further evaluation and suctioning of the bleeding lung. The BB should always be deflated under FOB vision. In 2006, Giannoni et al. [17] described a bilateral concurrent massive hemoptysis successfully controlled with the placement of more than one balloon catheter. Their patient was not intubated since a single-lumen tracheal tube could not allow the insertion of three devices (FOB and two blockers) inside the tube. They inserted each balloon through the nostrils.

A third alternative for the management of the airway during massive hemoptysis is the placement of a DLT, or endobronchial tube. These DLTs are specially designed for selective intubation of the right or left mainstem bronchi [18]. For massive hemoptysis, selective intubation of the left lung is preferable. The left-sided tube is easier to position than the right-sided tube which carries the risk of obstruction of the right upper lobe bronchus. DLTs have a bad reputation in the literature when used in the context of massive hemoptysis. Nevertheless, some of these publications are older [18] than the introduction of the “new” polyvinyl chloride DLTs whose positioning can be verified with the FOB. Other publications [1] refer to the use of DLTs for other conditions than massive hemoptysis and their conclusions cannot be used to determine the safety of DLTs during massive hemoptysis [19]. However, it has been demonstrated that anesthesiologists, with limited experience in thoracic anesthesia, frequently fail to successfully place lung isolation devices, DLTs or BBs [20].

When working in collaboration with thoracic anesthesiologists, it is our opinion that inserting a left-side DLT is a good strategy. The lumen to the nonbleeding lung is used to ventilate the patient. The other lumen, to the bleeding lung, permits passage of a pediatric FOB. These FOBs, with a diameter less than 4.2 mm, have a working channel allowing suction of blood and clots from the bleeding site. The lumen directed to the bleeding lung may be used to carry out a relatively “blind” and very careful catheter aspiration. With attentive care, the lumen may be cleared of blood or clots. The application of CPAP or mechanical ventilation with PEEP to the bleeding lung may help to decrease the bleeding and/or to improve the patient’s gas exchange.

Insertion of a DLT may be hazardous, even for an experienced anesthesiologist facing a hemorrhagic airway. Copious amounts of blood can make the use of FOBs quite difficult. A well-positioned DLT may easily be displaced during the frequent transfers of the patient from ICU to radiologic suites or frequent patient’s repositioning in bed. The author prefers to use left-side DLT with a carinal hook to stabilize the DLT onto the carina and fix it to the maxillary bone to minimize its displacement. Sometime, in face of massive hemoptysis, the use of a carinal hook helps to “blindly” place a DLT. It is important to note that BBs are at higher risk of dislodgement with movement or transfer of the patient than DLTs. Consequently, patients with a DLT or a BB in place should not be moved unless absolutely necessary and sometimes these patients should receive muscle relaxants [21, 22].

Once adequate lung isolation is achieved, the patient can be placed in the lateral decubitus position with the bleeding lung superior. The inferior, (nonbleeding) lung, will thus receive most of the pulmonary blood flow and this will help to control the hemorrhage, as it decreases the perfusion in the upper lung. This position will also improve ventilation/perfusion matching. The patient should be ventilated with 100% oxygen and PEEP should be applied to the inferior lung (nonbleeding) in order to improve gas exchange. PEEP or CPAP may also be used on the upper (bleeding) lung acting for a hemostatic effect and to help gas exchange.

Diagnostic Tools and Therapeutic Approaches

There is a controversy concerning the sequence of radiological interventions. Initial CT scan is thought to shorten examination time, but in a patient with massive hemoptysis etiologic diagnosis is less important than immediate interruption of the bleeding process by beginning with angiography [23].

Chest radiography is readily available and is an important diagnostic tool in finding the cause of bleeding, comparing it with prior films, if possible, and localizing pulmonary pathology. High definition computed tomographic (HDCT) scanning angiography is an excellent diagnostic tool. Except for life-threatening situations, CT should be performed before the bronchoscopic exploration. CT has superior diagnostic capacity over bronchoscopy and chest radiography for demonstrating underlying pathology and the site of bleeding in hemoptysis, especially in bronchiectasis, bronchogenic carcinoma, and aspergilloma cases [8, 10]. Vascular pathologies such as arteriovenous malformation or aneurysm, which are rare causes of hemoptysis, are also depicted very clearly in contrast-enhanced CT examinations [11]. With recent developments in multidetector CT technique, it is now possible to scan the whole thorax into very thin slices (1.25 mm) in a very short time (12–15 s) [12, 13]. Both the lesion causing hemoptysis and bronchial and nonbronchial systemic

feeding arteries are detected during the same study using 80–100 mL of contrast medium. In angiography-controlled studies, 86–87% of the pathologic vessels detected by invasive angiography were also discovered with CT angiography (CTA) [12, 13].

Bronchoscopy

For a patient presenting with massive hemoptysis, the medical team may choose to proceed with early or late bronchoscopy. This bronchoscopy may be rigid or flexible and its primary goal is to localize the site or at least lateralize the side of the bleeding source. The secondary goal is to clear the airway of gross blood. Finally, the third goal may be to use a therapeutic agent to control the bleeding. If the situation is not critical, a quick trial of FOB can be performed to determine the origin or at least the side of the bleeding. If the patient's oxygenation is significantly compromised or the bleeding continues at a brisk pace, elective oral intubation with an endotracheal tube (8.0 mm or larger) should be performed; this may be done simultaneously with the bronchoscopy.

Timing

Although most authorities advocate bronchoscopy to help localize bleeding during massive hemoptysis, the moment when to use the bronchoscopy is still controversial [10]. In the literature, it is frequently mentioned that patients with massive hemoptysis require urgent bronchoscopy. The argument for this assertion is that bleeding will increase with time, making visualization difficult. It is reported that bronchoscopy helps to detect the bleeding site in a lung or lobe in patients with diffuse pulmonary disease [9].

More recently a new option is emerging. Patients presenting with massive hemoptysis are immediately directed to the angiographic suite to get a diagnostic angiogram and BAE at the same time. Patients at risk of asphyxia prior to the BAE benefit from lung isolation techniques. The FOB is then carried out later. The main argument for this sequence is that during the acute phase of severe massive hemoptysis, the airways are filled with large volumes of blood restricting the use of bronchoscopy and consequently impeding endobronchial treatment [7, 26]. Sometimes, endoscopic examination may aggravate bleeding and delay more effective treatment. Hsiao et al. reported, in 2001 [26], that bronchoscopy was not a prerequisite in the treatment process considering the risk of airway compromise from sedation, delay in definitive treatment, hypoxemia, and high cost. In this study, bronchoscopy findings were taken into consideration whenever they were available. Not having to perform a bronchoscopy did not affect the progress of endovascular treatment. Bronchoscopy findings have not altered the course of angiography and endovascular treatment in any of their patients.

Flexible bronchoscopy successfully localized the site of bleeding in 26 patients. In comparison, chest radiographs localized the bleeding site in 23 patients. This suggests that flexible bronchoscopy is effective at identifying the site of bleeding in patients with massive hemoptysis, but localizing a radiographic abnormality is sufficiently accurate to warrant proceeding to BAE without bronchoscopy [24].

Despite the "lack of proof" that early bronchoscopy is beneficial, the general expert consensus favors an early bronchoscopy, especially for patients with massive hemoptysis [3]. The early procedure provides clinicians with the maximal amount of information upon which to base future decisions, particularly in patients who develop sudden recurrence or acceleration of their bleeding. Nevertheless, early bronchoscopy has not been strictly proven to improve outcome.

Practically speaking, early bronchoscopy should be done within the first 12–18 h for the patient who is clinically stable or for whom bleeding has become quiescent. Alternatively, bronchoscopy is performed as early as it is safely feasible on the unstable, decompensating patient [24]. In some institutions, in patients with massive hemoptysis who are unstable, diagnostic angiography is the preferred imaging method to localize the bleeding site because it allows for immediate treatment [27].

Type of Bronchoscopy

Depending on each institution's preference, rigid and/or flexible bronchoscopes are used to evaluate and to stabilize any patient presenting massive hemoptysis. The selection is likely to reflect the institution's or the user's experience [10]. No study addresses this issue.

Rigid

Rigid bronchoscopy has been, until recently, the procedure of choice after initial chest radiography. Many surgeons and much of the older literature strongly advocate the use of the rigid bronchoscope. Rigid bronchoscopy is preferred because of its ability to suction large quantities of liquid and clotted blood, to use a great variety of therapies during bronchoscopy, such as direct cauterization or packing of bronchial lesions, and to continuously provide ventilation. Obviously, operating room setting and general anesthesia are required. The distal range of inspection in the bronchial tree is significantly reduced compared to the FOB.

Over time, the technique of rigid bronchoscopy is being less and less used and, as a result, is not available in many institutions [11]. Consequently, a rigid bronchoscope is usually used for patients with ongoing massive hemoptysis after an inadequate bedside FOB. The flexible bronchoscope can also be used in conjunction with the rigid bronchoscope by passing it through its lumen. This allows a better examination of the more distal and the upper lobe airways [24].

A survey in 1998 noted that 79% of physicians treating massive hemoptysis favored the flexible optic bronchoscope (FOB) as the initial technique compared to 48% in a similar survey performed in 1988 [28, 29].

Flexible

FOB has become more acceptable as an initial procedure for intubated or nonintubated patients. The main limitation of FOB compared to the rigid bronchoscope is its limited ability to produce adequate suction through its smaller port. Also, with massive hemoptysis, the presence of blood in the inferior airway may absorb the light transmitted by the FOB and consequently decrease visualization [11].

For maximal safety, most patients should be intubated when bronchoscopy is indicated in presence of massive hemoptysis. If bleeding accelerates or recurs during the procedure, the bronchoscope can be removed, and suction can be applied while controlling the airway. The view obtained through the bronchoscope is commonly obscured by clots on the tip of the scope; thus, it is important to be able to safely remove the scope, clean the tip and suction the channel to continue the examination [24].

Endobronchial Therapy

Laser photocoagulation or resection, electrocauterization, and cryotherapy are useful tools for minor or moderate hemoptysis. Unfortunately, these techniques are rarely efficient against massive hemoptysis [11]. If bronchoscopy allows visualization of a localized bleeding mucosal lesion, laser therapy or electrocauterization may be considered, if available. Both techniques can be used through a flexible or rigid bronchoscope. Since excellent visualization of the bleeding site is required, the rigid bronchoscope may be preferred because of its better suction capability.

Pharmacologic Adjuncts

Some pharmacologic adjuncts may be used through the FOB. Topical agents such as warm saline may initially help to break down gross clots and identify the bleeding site [11]. Having isolated the bleeding site, initial control may be obtained by using 50 mL sequential aliquots of ice-saline lavage, up to 500 mL [10]. Topical epinephrine (1:20,000) is used to locally vasoconstrict bleeding vessels. Thrombin, fibrinogen-thrombin, or fibrin-precursor solutions can be injected as hemostatic agents via intrabronchial infusion through a catheter inserted into a FOB wedged against the bleeding bronchus [30, 31].

As described earlier, BBs may be inserted into a bleeding bronchus under the control of a FOB to obtain an endobronchial tamponade. When a lesion is not amenable to embolization, as there are no feeding vessels, and if surgical resection is not thought to be a viable option, the best way to protect the contra-lateral lung may be the insertion of a lung isolation device.

But this measure may offer only a temporary relief. At that time, the use of self-expanding airway stent to cover over a bleeding segmental bronchial orifice may act as both tamponade and isolation of the bleeding source [32].

Systemic Therapy

Intravenous vasopressin has been used to treat massive hemoptysis, in a fashion similar to its use in gastrointestinal hemorrhage [33]. It should be discontinued before BAE, if possible [34–36]. Other therapies that may promote coagulation and that have been used successfully for massive hemoptysis include, intravenous estrogens (Premarin®), desmopressin (DDAVP), ADH (vasopressin), tranexamic acid (Cyclokapron®) [37–40], and recombinant activated coagulation Factor VII [41].

Bronchial Artery Embolization (BAE)

First reported by Remy et al. in 1973 [7], the use of BAE for management of massive hemoptysis has become widespread. It has become the main option for the treatment of massive hemoptysis, either at first presentation or in case of recurrence. Development of BAE has been a huge advance in treatment of patients with massive hemoptysis, both as a temporizing measure and as a definitive treatment for some patients [42]. After a number of improvements, it is now the procedure of choice in all patients except those immediately exsanguinating [6]. It is now considered the most effective nonsurgical treatment in massive hemoptysis [1]. In the hands of experienced angiographers, embolization successfully stops bleeding more than 85% of the time, especially if the bronchial circulation and the systemic arterial supply are carefully defined [20, 21].

Multiple imaging modalities are used to confirm the diagnosis and to locate the bleeding site in stable patients. These include plain chest radiography, chest computed tomography and bronchoscopy. But in patients with massive hemoptysis who are unstable, diagnostic angiography is the preferred imaging method for localizing the bleeding site because it allows for immediate treatment [27].

The initial step for transcatheter embolization is performing a thoracic angiogram to visualize and localize all the main systemic arteries to the lung(s). Once the feeding arteries are localized, selective bronchial arteriography is performed to characterize the bleeding vessel. Once the bleeding vessel is identified, an embolic agent is used. Postembolization bronchial arteriogram and thoracic aortogram are performed to ensure the complete blockage of all the feeding arteries with no further bleeding from vessels. Immediate recurrent hemoptysis often occurs due to missed feeding arteries that went untreated, whereas later recurrence may take place as a result of collateralization or recanalization of either the feeding artery or new bleeding vessels [27].

Multiple publications (10 series including 609 patients, from 1983 to 2007) have demonstrated an immediate success rate of controlled bleeding between 70 and 95% with a

recurrence rate between 13 and 43%. These studies also report a minimal immediate complication rate of less than 1% [27]. The most serious complication of BAE is the accidental embolization of the anterior spinal artery (Adamkiewitz) either by contrast material or the embolizing particles causing ischemic injuries [1]. The anterior spinal artery originates from a bronchial artery in about 5% of patients. The reported incidence of this complication has been described as 1% [43]. This risk has been decreased by superselective embolization techniques using smaller catheters that can be placed distally [44]. Renal dysfunction resulting from the contrast load is a concern, especially in patients who are hemodynamically unstable due to blood loss [6].

Correct clinical evaluation and ventilation stabilization of the patient are mandatory before BAE in massive hemoptysis [23]. Intubating a patient with a single- or double-lumen tube helps to monitor, with the aid of FOB, the interruption of bleeding through a radiologic intervention and to clean the inferior airways from any residual blood and clots.

Surgery

Historically, pulmonary resection has been the most effective method to control and prevent recurrent bleeding [6]. Comparing the results with those of medical or surgical management is difficult for several reasons. The criteria of eligibility for surgery differ among institutions and seem to be subject to surgical or institutional bias [1]. The primary problem is selection bias – that is, patients who are more likely to die are less likely to be operated on [6].

Patients with lateralized, ideally well-localized, uncontrollable bleeding should be assessed early for possible surgery in case bleeding remains brisk and unresponsive to other measures. Surgery is reserved as an absolute last resort for operative candidates not salvageable by embolotherapy [6].

Patients presenting massive hemoptysis are too ill for physiologic testing, historical data are therefore used to estimate the patient's ability to undergo lung resection. Relative contraindications to surgery include severe underlying pulmonary disease, active TB, diffuse underlying lung disease (cystic fibrosis, multiple AVMs, multifocal bronchiectasis), and diffuse alveolar hemorrhage.

Morbidity and mortality are significantly greater with emergent surgery for persistent massive bleeding compared to elective surgery in nonbleeding patients. In most series of emergent therapy, surgical mortality for treatment of massive hemoptysis is approximately 20%, ranging from 10 to 38% for series published between 2000 and 2003 [45–47], with morbidity occurring in an additional 25–50% of patients; however, most of these series are more than 20 years old.

The reasons for such high mortality and morbidity may be related to ongoing bleeding in unstable hemodynamic conditions, together with soiling of other healthy bronchopulmonary segments before and during the operation. Contamination of the contra-lateral lung before, during, and after surgery is

a main cause of postoperative respiratory failure leading to prolonged ventilation, nosocomial pneumonia, and death [6]. Solutions are to delay the surgery with BAE, to obtain hemodynamic stability preoperatively and to perform bronchial toilet pre and postoperatively. Before the critical decision to perform surgery, the surgeons should make sure that available interventional modalities such as balloon BBs, rigid bronchoscopy, or BAE could be used in an optimal manner to buy time so as to delay surgery for a better surgical outcome.

Iatrogenic Pulmonary Artery Rupture

The use of a pulmonary artery catheter (PAC) is becoming less frequent in the operating room since the general use of trans-esophageal echocardiography. Nevertheless, the PAC remains a useful tool for diagnosis and management of many patients with cardiac or lung diseases. Sicker patients may need the insertion of a PAC and these sicker patients are usually the patients most at risk for catheter-induced pulmonary artery rupture (PAR). Prevention is the first approach to develop when confronted with an iatrogenic complication. The first step of prevention is judicious selection of the patient. The second is the appropriate use and management of the PAC. But when a catheter-induced PAR occurs, the physician needs to have a clear scheme of intervention to deal with this severe complication [48].

In fact, the incidence of rupture is not very high, with an average of 0.01–0.47%. In a large retrospective study of patients with a Swan-Ganz catheter, Kearney and Shabot [49] found an incidence of PAR of 0.031% and a mortality of 70%. The mortality rate of PAR averages 50%, but can be as high as 75% in anticoagulated patients. Death occurs most often secondary to asphyxia. If there is a delay before appropriate management is instituted, it will contribute to a higher mortality rate. Risk factors for catheter-induced PAR include female gender, age over 60 years, improper catheter placement, and preexisting pulmonary hypertension.

The initial presentation may be as obvious as massive pulmonary hemorrhage or as subtle as a minor hemoptysis associated with cough, or it may be totally asymptomatic [50]. Moreover, any hemoptysis in the presence of a PAC should be investigated because of the high suspicion of PAR or false aneurysm formation.

The proposed mechanisms for catheter-induced PAR include catheter tip lodged in the vessel wall when a PAC is advanced while the balloon is not inflated or when eccentric balloon inflation exposes the catheter tip and guides it into the arterial wall or migration of catheter into a smaller arteriole with subsequent rupture caused by balloon inflation. Primary management of catheter-induced PAR focuses on the prevention of asphyxia secondary to lung spillage. Prevention of contamination of the unaffected lung is essential.

Management will differ depending of the clinical presentation, mainly in which setting it is presenting: (1) in the ICU,

(2) in the operating room, or (3) in the radiological suite. Management of the airway for lung isolation follows the same rules as for any massive hemoptysis, as described before.

Intensive Care Unit Setting

When a PAC is inserted and there is hemoptysis, whether it is massive or negligible, a chest radiograph is usually obtained and will show infiltration around the catheter tip or pleural effusion. The side of a PAC may serve as a guide to determine which side the hemorrhage may come from. Since most PACs are located in the right lung (90%), mainly the right lower lobe, it can be assumed that hemorrhage comes from the right side if the situation is critical [51].

It has been suggested that a PAC could be deflated, withdrawn a few centimeters and left in the pulmonary artery. The balloon may be inflated in order to compress the bleeding vessel or to temporarily obstruct the feeding artery [52]. We recommend that this technique should be used only with the aid of fluoroscopy to finely adjust the position of the balloon in order to avoid malposition of the balloon. Improper positioning may augment the bleeding by increasing the vascular laceration or by diverting the pulmonary blood flow to the injured vessel.

With a stable patient or when the diagnosis remains unclear, a contrast-enhanced HDCT-scan can be performed since it is a valuable diagnostic tool. It can confirm the possibility of a pulmonary artery false aneurysm (PAFA) but also exclude any other causes of hemoptysis. CT-scan is usually followed by an angiography with embolization if indicated and feasible (see Table 34.3).

Operating Room Setting

If a hemorrhage happens during surgery, lung isolation can be rapidly achieved and the diagnostic and therapeutic procedures started while the patient is under anesthesia. If the

Fig. 34.1. Flow diagram of management of massive hemoptysis during weaning from cardiopulmonary bypass. *CPB* cardio-pulmonary bypass; *ETT* endotracheal tube; *PA* pulmonary artery; *FOB* fiberoptic bronchoscopy; *Paren.* lung parenchyma.

TABLE 34.3. Management of a pulmonary artery catheter.

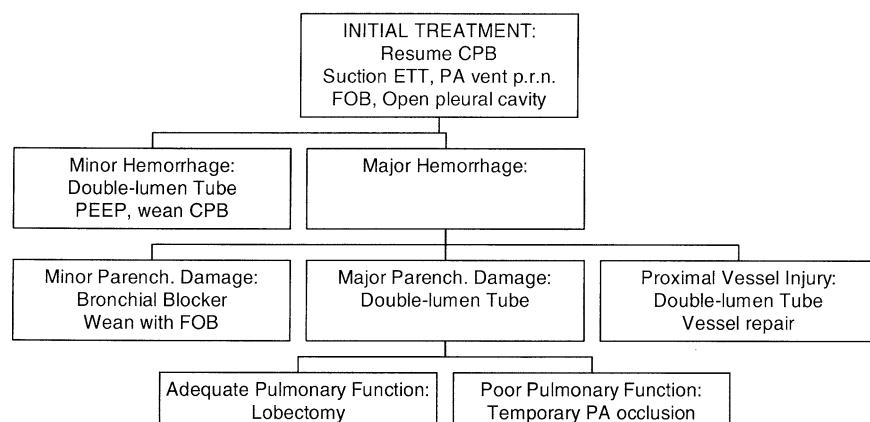
Induced pulmonary hemorrhage
1. Initially place the patient with the nonisolated, bleeding lung in the inferior position
2. Endotracheal intubation, oxygenation, airway toilet
3. Lung isolation: endobronchial double- or single-lumen tube or bronchial blocker
4. Withdraw the pulmonary artery catheter several centimeters, leaving it in the main pulmonary artery. Do not inflate the balloon (except with fluoroscopic guidance)
5. Position the patient with the isolated bleeding lung nondependant. PEEP to the bleeding lung if possible
6. Transport to medical imaging for diagnosis and embolization if feasible

hemoptysis happens before the principal period of the surgery, elective surgery has to be postponed until the PAR is investigated and stabilized. During cardiac surgery, when a hemorrhage happens after cardio-pulmonary bypass (CPB), but before heparin reversal, CPB should be reinstated to bypass the lung circulation and stop the bleeding (see Fig. 34.1). An alternative have been recently published by Bianchini et al. in 2007 [53]. They suggest prompt institution of ECMO circulatory support by a simple shunting from the CPB circuit. Either alternative gives the anesthesiologist time to isolate the lungs and maximize oxygenation. If the hemoptysis begins after protamine administration, the best conduct is to finish the surgery as quickly as possible, isolate the lung, and proceed to a definite investigation and treatment of the PAR.

Radiological Setting

During cardiac catheterization, the PAC can be used to evaluate pulmonary vascular resistance and the wedge pressure. When catheter-induced PAR happens in this setting, it is relatively easy to pull back the PAC a few centimeters and to reinflate the balloon under direct observation. Thus, it may be possible to stop the bleeding pending further radiological

Management of Pulmonary Hemorrhage During Weaning from Cardio-Pulmonary Bypass:



intervention. However, this measure does not always enable us to contain the hemorrhage [54]. This is the reason why we recommend using fluoroscopy and contrast injection to confirm that the PAC is still proximal to the injured vessel and that balloon inflation impedes flow through the lacerated vessel. Diagnostic angiography and embolization can be easily performed at that point. This may permit avoiding, in certain circumstances, intubation, lung isolation, and postprocedure ventilation [55].

Pulmonary Artery False Aneurysm (PAFA)

PAFA formation is secondary to the accumulation of blood in an aneurismal sac compressed by the lung parenchyma. While there is no intact vessel wall lining containing the bleeding, the lung parenchyma may prevent further extravasation. The presence of a PAFA requires intervention, because one can never be certain that spontaneous healing will occur. Delayed pulmonary hemorrhage occurs in 30–40% of cases of a PAFA caused by a previous catheter-induced PAR. Rebleeding can occur as late as 2 weeks to 7 months after the initial event [56].

If there is suspicion of a PAFA on the CT-scan, an angiogram should be done. When the clinical suspicion of PAR is high or when the patient is unstable, angiography remains the procedure of choice because it allows both diagnostic and therapeutic intervention [57]. If diagnosis of a PAFA is confirmed, selective embolization helps to reduce morbidity and mortality. Embolization is successful in 75% of cases, with a rebleeding rate of about 20%. Sometimes, it can be deleterious to embolize the PAFA in regard to global lung function. In

these cases conservative treatment can be tried. Follow up of this type of patients with repeat contrast CT-scan is required.

With radiological intervention, there is less and less place for surgery in the context of catheter-induced PAR (see Fig. 34.2). Surgery, including pulmonary artery ligature, segmentectomy, lobectomy or pneumonectomy, is reserved for extreme cases since it is technically challenging with a high morbidity [56]. Since the morbidity and mortality of radiological intervention are less than traditional surgery, it should be tried first [58]. However, a proximal vascular injury may be an indication for performing lung surgery primarily [59].

Posthemoptysis Evolution

Following massive hemoptysis, treated either by endoscopy, radiological intervention or surgery, it is important to perform a bronchoscopy to clean the tracheo-bronchial tree to remove any blood and clots in the distal airway. This action will help promote better and faster patient recuperation.

Posttracheostomy Hemorrhage

Another clinically challenging scenario involving massive airway bleeding is posttracheostomy hemorrhage. Hemorrhage in the immediate postoperative period following a tracheostomy is usually from local vessels in the incision such as the anterior jugular or inferior thyroid veins. Massive hemorrhage 1–6 weeks postoperatively is most commonly due to tracheo-innominate artery fistula [60]. A small sentinel bleed occurs in most patients before a massive bleed. The management protocol for tracheo-innominate artery fistula is outlined in Table 34.4.

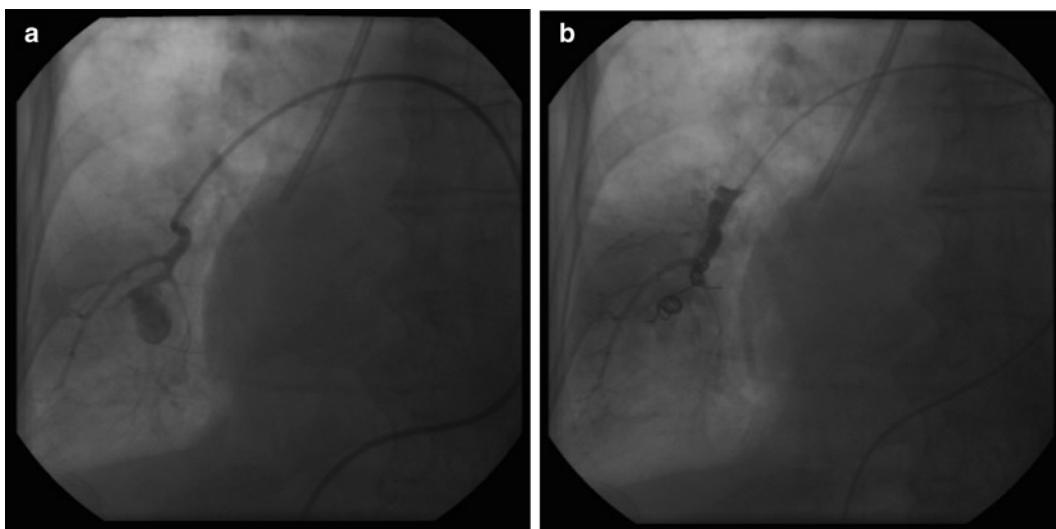


FIG. 34.2. (a) Radiographic contrast dye injection showing a false aneurysm of the pulmonary artery of the right lower lobe following massive hemoptysis induced by pulmonary artery catheter rupture. (b) A coil has been placed by interventional radiology in the false aneurysm of the right lower pulmonary artery in the same patient. Dye injection shows that the aneurysm has embolized with no further leakage.

TABLE 34.4. Management of tracheo-innominate artery fistula hemorrhage.

1. Over-inflate the tracheostomy cuff to tamponade the hemorrhage
If this fails
2. Replace the tracheostomy tube with an oral endotracheal tube. Position the cuff with FOB guidance just above the carina
3. Digital compression of the innominate artery against the posterior sternum using a finger passed through the tracheostomy stoma
If this fails
4. Slow withdrawal of the ETT and over-inflation of the cuff to tamponade
5. Then proceed with definitive therapy: sternotomy and ligation of the innominate artery

Conclusion

Endobronchial control measures and artery embolization have radically changed the management of massive hemoptysis. With control of hemorrhage, nonsurgical patients can be identified and surgical candidates accurately assessed to allow an elective operation, with lower morbidity and mortality, if conservative measures are unsuccessful [6].

Based on the above data, the following is a reasonable approach to the patient with massive hemoptysis. First, stabilize the patient's oxygenation, ventilation, and hemodynamic status. Early correction of coagulopathy and consultation with critical care physician, pulmonary medicine (bronchoscopist), interventional radiologist, thoracic surgery, and anesthesiologist are essential. Perform early bronchoscopy along with other appropriate diagnostic studies. If the patient continues to bleed aggressively, arteriography is most reasonable for localization and therapy. If bleeding persists despite embolization or if the patient is too ill to go to angiography, then blockade therapy or insertion of a double-lumen tube should be considered in preparation for rigid bronchoscopy in the operating room with possible lung resection if warranted. While surgery remains the only truly definitive therapy, it should not be used in the acute emergent setting unless it cannot be avoided.

In conclusion, in experienced hands, BAE is an effective therapeutic tool and plays a pivotal role in the management of life-threatening massive hemoptysis. Surgery is the only curative treatment and is especially effective for localized lesions, and should be considered when BAE is unavailable or bleeding is unlikely to be controlled by that approach.

Clinical Case Discussion

A young woman, 26 years old, is well known in our institution for Eisenmenger's syndrome secondary to complex heart disease. She had a patent ductus arteriosus for which no surgical option was available when diagnosed at 4 years old. She was referred to our center 4 years ago for pulmonary hypertension. At that time, it was observed that the right pulmonary artery originates directly from the aorta. She has been treated with Flolan (epoprostenol) continuous intravenous infusion for 3 years.

A few months ago, she presented some episodes of moderate hemoptysis treated with the aid of BAE. Six days before, she presented a new moderate hemoptysis necessitating BAE. She was observed in an intensive care unit and after 5 days without bleeding, she was transferred to the bronchoscopy suite to look for a clot occluding the right lower lobe bronchus. With the aid of sedation and local anesthesia, the area was easily approached. The clot was dislodged partially without any problem. Trying to dislodge the rest of the clot provoked coughing and induced massive bleeding from the inferior lobe.

Questions

Which immediate procedure should be undertaken?

1. Nasal oxygen was already in place for the FOB exam.
2. Right lateral decubitus position to protect the left lung from blood spillage.
3. Irrigation to the origin of bleeding with cold saline.

Bleeding continues and become massive hemoptysis. What is the next step?

4. Left side endobronchial intubation with single-lumen tube with the assistance of the FOB.
5. Left lateral decubitus position to improve left lung gas exchange and minimize bleeding from right side lung.

The patient was directed, with anesthesia assistance, to the radiological suite for angiography and BAE as needed. Following diagnostic angiography and therapeutic embolization, the radiologist would like to know if the bleeding continues from the right lung. What we can do to help her?

6. Replace the endobronchial single-lumen tube with a DLT and perform FOB with a pediatric FOB via the DLT.

Following this procedure, we aspirated the right lung bronchial tree. At that time, we identified active bleeding originating from right lower lobe superior segmental bronchus. Following a repeat BAE, the bleeding ceased and we terminated the cleaning of the bilateral bronchial tree without finding any other bleeding site.

The patient was transferred to the ICU with her DLT in place. She was sedated and ventilated until the next morning when she was extubated. She did not present any recurrence and she was transferred to another center for evaluation for lung transplantation.

References

1. Jean-Baptiste E. Clinical assessment and management of massive hemoptysis. *Crit Care Med.* 2000;28(5):1642–7.
2. Amirana M et al. An aggressive surgical approach to significant hemoptysis in patients with pulmonary tuberculosis. *Am Rev Respir Dis.* 1968;97(2):187–92.
3. Bobrowitz ID, Ramakrishna S, Shim YS. Comparison of medical v surgical treatment of major hemoptysis. *Arch Intern Med.* 1983;143(7):1343–6.

4. Corey R, Hla KM. Major and massive hemoptysis: reassessment of conservative management. *Am J Med Sci.* 1987;294(5):301–9.
5. Garzon AA, Cerruti MM, Golding ME. Exsanguinating hemoptysis. *J Thorac Cardiovasc Surg.* 1982;84(6):829–33.
6. Wigle DA, Waddell TK. Investigation and management of massive hemoptysis. In: Pearson's thoracic and esophageal surgery. Elsevier: Toronto; 2008. Chapter 38.
7. Remy J et al. Treatment, by embolization, of severe or repeated hemoptysis associated with systemic hypervascularization. *Nouv Presse Med.* 1973;2(31):2060.
8. Hiebert CA. Balloon catheter control of life-threatening hemoptysis. *Chest.* 1974;66(3):308–9.
9. Fraser KL et al. Transverse myelitis: a reversible complication of bronchial artery embolisation in cystic fibrosis. *Thorax.* 1997;52(1):99–101.
10. Dweik RA, Stoller JK. Role of bronchoscopy in massive hemoptysis. *Clin Chest Med.* 1999;20(1):89–105.
11. Karmy-Jones R, Cuschieri J, Vallieres E. Role of bronchoscopy in massive hemoptysis. *Chest Surg Clin N Am.* 2001;11(4):873–906.
12. Wedzicha JA, Pearson MC. Management of massive haemoptysis. *Respir Med.* 1990;84(1):9–12.
13. Campos JH. Progress in lung separation. *Thorac Surg Clin.* 2005;15(1):71–83.
14. Spicak-Macan J et al. Exsanguinating tuberculosis-related hemoptysis: bronchial blocker introduced through percutaneous tracheostomy. *Minerva Anestesiol.* 2009;75(6):405–8.
15. Maguire MF et al. Catastrophic haemoptysis during rigid bronchoscopy: a discussion of treatment options to salvage patients during catastrophic haemoptysis at rigid bronchoscopy. *Interact Cardiovasc Thorac Surg.* 2004;3(2):222–5.
16. Freitag L et al. Three years experience with a new balloon catheter for the management of haemoptysis. *Eur Respir J.* 1994;7(11):2033–7.
17. Giannoni S et al. Bilateral concurrent massive hemoptysis successfully controlled with double endobronchial tamponade. A case report. *Minerva Anestesiol.* 2006;72(7–8):665–74.
18. Gourin A, Garzon AA. Operative treatment of massive hemoptysis. *Ann Thorac Surg.* 1974;18(1):52–60.
19. Klein U et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia: a prospective study. *Anesthesiology.* 1998;88(2):346–50.
20. Campos JH, et al. Devices for lung isolation used by anesthesiologists with limited thoracic experience: comparison of double-lumen endotracheal tube, Univent torque control blocker, and Arndt wire-guided endobronchial blocker. *Anesthesiology.* 2006;104(2):261–6; discussion 5A.
21. Campos JH. Which device should be considered the best for lung isolation: double-lumen endotracheal tube versus bronchial blockers. *Curr Opin Anaesthesiol.* 2007;20(1):27–31.
22. Narayanaswamy M et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. *Anesth Analg.* 2009;108(4):1097–101.
23. de Gregorio MA et al. Hemoptysis workup before embolization: single-center experience with a 15-year period follow-up. *Tech Vasc Interv Radiol.* 2007;10(4):270–3.
24. Ingbar DH. Overview of massive hemoptysis. UpToDate, 2010, December 1st.
25. Poyanli A et al. Endovascular therapy in the management of moderate and massive haemoptysis. *Br J Radiol.* 2007;80(953):331–6.
26. Hsiao EI et al. Utility of fiberoptic bronchoscopy before bronchial artery embolization for massive hemoptysis. *AJR Am J Roentgenol.* 2001;177(4):861–7.
27. Lee EW et al. Bronchial and pulmonary arterial and venous interventions. *Semin Respir Crit Care Med.* 2008;29(4):395–404.
28. Haponik EF, Chin R. Hemoptysis: clinicians' perspectives. *Chest.* 1990;97(2):469–75.
29. Lippmann ML, Walkenstein MD, Goldberg SK. Bronchoscopy in hemoptysis. *Chest.* 1990;98(6):1538.
30. Tsukamoto T, Sasaki H, Nakamura H. Treatment of hemoptysis patients by thrombin and fibrinogen-thrombin infusion therapy using a fiberoptic bronchoscope. *Chest.* 1989;96(3):473–6.
31. Bense L. Intrabronchial selective coagulative treatment of hemoptysis. Report of three cases. *Chest.* 1990;97(4):990–6.
32. Brandes JC, Schmidt E, Yung R. Occlusive endobronchial stent placement as a novel management approach to massive hemoptysis from lung cancer. *J Thorac Oncol.* 2008;3(9):1071–2.
33. Magee G, Williams Jr MH. Treatment of massive hemoptysis with intravenous pitressin. *Lung.* 1982;160(3):165–9.
34. Mal H et al. Immediate and long-term results of bronchial artery embolization for life-threatening hemoptysis. *Chest.* 1999;115(4):996–1001.
35. Remy J et al. Treatment of hemoptysis by embolization of bronchial arteries. *Radiology.* 1977;122(1):33–7.
36. Stoller J. Diagnosis and management of massive hemoptysis: a review. *Respir Care.* 1992;37:564–81.
37. Bilton D et al. Life threatening haemoptysis in cystic fibrosis: an alternative therapeutic approach. *Thorax.* 1990;45(12):975–6.
38. Chang AB et al. Major hemoptysis in a child with cystic fibrosis from multiple aberrant bronchial arteries treated with tranexamic acid. *Pediatr Pulmonol.* 1996;22(6):416–20.
39. Graff GR. Treatment of recurrent severe hemoptysis in cystic fibrosis with tranexamic acid. *Respiration.* 2001;68(1):91–4.
40. Popper J. The use of premarin IV in hemoptysis. *Dis Chest.* 1960;37:659–60.
41. Tien HC et al. Successful use of recombinant activated coagulation factor VII in a patient with massive hemoptysis from a penetrating thoracic injury. *Ann Thorac Surg.* 2007;84(4):1373–4.
42. Johnson JL. Manifestations of hemoptysis. How to manage minor, moderate, and massive bleeding. *Postgrad Med.* 2002;112(4):101–6; 108–9; 113.
43. Zhang JS et al. Bronchial arteriography and transcatheter embolization in the management of hemoptysis. *Cardiovasc Interv Radiol.* 1994;17(5):276–9.
44. Tanaka N et al. Superselective bronchial artery embolization for hemoptysis with a coaxial microcatheter system. *J Vasc Interv Radiol.* 1997;8(1 Pt 1):65–70.
45. Lee TW et al. Management of massive hemoptysis: a single institution experience. *Ann Thorac Cardiovasc Surg.* 2000;6(4):232–5.
46. Knott-Craig CJ et al. Management and prognosis of massive hemoptysis. Recent experience with 120 patients. *J Thorac Cardiovasc Surg.* 1993;105(3):394–7.
47. Endo S et al. Management of massive hemoptysis in a thoracic surgical unit. *Eur J Cardiothorac Surg.* 2003;23(4):467–72.
48. Bussieres JS. Iatrogenic pulmonary artery rupture. *Curr Opin Anaesthesiol.* 2007;20(1):48–52.

49. Kearney TJ, Shabot MM. Pulmonary artery rupture associated with the Swan-Ganz catheter. *Chest*. 1995;108(5):1349–52.
50. Poplausky MR et al. Swan-Ganz catheter-induced pulmonary artery pseudoaneurysm formation: three case reports and a review of the literature. *Chest*. 2001;120(6):2105–11.
51. Stratmann G, Benumof JL. Endobronchial hemorrhage due to pulmonary circulation tear: separating the lungs and the air from the blood. *Anesth Analg*. 2004;99(5):1276–9.
52. Dopfmer UR, et al. Treatment of severe pulmonary hemorrhage after cardiopulmonary bypass by selective, temporary balloon occlusion. *Anesth Analg*. 2004;99(5):1280–2; table of contents.
53. Bianchini R et al. Extracorporeal membrane oxygenation for Swan-Ganz induced intraoperative hemorrhage. *Ann Thorac Surg*. 2007;83(6):2213–4.
54. Gottwaldes Y, Wunschel-Joseph ME, Hanssen M. Coil embolization treatment in pulmonary artery branch rupture during Swan-Ganz catheterization. *Cardiovasc Intervent Radiol*. 2000;23(6):477–9.
55. Fortin M et al. Catheter-induced pulmonary artery rupture: using occlusion balloon to avoid lung isolation. *J Cardiothorac Vasc Anesth*. 2006;20(3):376–8.
56. Mullerworth MH et al. Recognition and management of catheter-induced pulmonary artery rupture. *Ann Thorac Surg*. 1998;66(4):1242–5.
57. Utsumi T et al. Swan-Ganz catheter-induced pseudoaneurysm of the pulmonary artery. *Jpn J Thorac Cardiovasc Surg*. 2002;50(8):347–9.
58. Ingbar D. Life threatening hemoptysis. In: Shoemaker W, editor. *Textbook of critical care*. 4th ed. Philadelphia: WB Saunders; 1515.
59. Chauhan S et al. Case 6 – 2001: exsanguinating endotracheal hemorrhage during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*. 2001;15(3):377–80.
60. Grant CA, Dempsey G, Harrison J, Jones T. Tracheo-innominate artery fistula after percutaneous tracheostomy: three case reports and a clinical review. *Br J Anaesth*. 2006;96:127–30.

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Key Points

- Patients with pulmonary alveolar proteinosis have a restrictive disease and are hypoxic.
- Lavage of one lung with large quantities of saline requires careful lung isolation.
- For more than 10 years, bilateral lung lavage has been performed during the same anesthetic period.
- GM-CSF associated therapy is now a complementary treatment to WLL for pulmonary alveolar proteinosis, when needed.

Introduction

This chapter reviews the historical considerations of whole lung lavage (WLL), when its performance is appropriate, details of the technique, complications, and finally benefits of this unusual treatment modality. It is important to differentiate WLL from bronchoalveolar lavage (BAL). BAL is a diagnostic tool performed with the aid of a fiberoptic bronchoscope (FOB) under local anesthesia, which uses only 300 cc of liquid in one segment of the lung. WLL is a treatment modality that requires over 10 L of normal saline instilled through a double-lumen tube in one whole lung while the patient is under general anesthesia.

Historical Considerations

WLL was first described in 1928 [1]. In the early 1960s, the first application of this technique was used to treat pulmonary alveolar proteinosis (PAP) [2–5]. At that time, the procedure consisted in repeated segmental flooding through a percutaneous transtracheal catheter positioned blindly in the bronchial tree. This technique was performed in an awake patient and was repeated four times a day for 2–3 weeks, using physical positioning to direct the saline sequentially into different lung segments. The 1980–2000 period lead to the development of a modern technique of unilateral WLL, which is carried out under general anesthesia and lung separation [6–8]. Since the beginning of the century, performing bilateral WLL during the same anesthesia period is the procedure of choice. Parallel with this evolution, the pathogenesis of WLL has been better defined since the discovery of the role of *granulocyte macrophage-colony stimulating factor* (GM-CSF) in surfactant catabolism.

Indications

Until recently, WLL was the most effective proven treatment modality for symptomatic PAP. This rare and enigmatic lung disease is caused by an alveolar accumulation of a lipoproteinaceous material. The alveolar material is composed principally

of surfactant phospholipids and apoproteins. The presence of this material creates a real alveolocapillary blockade. This pathology produces little or no lung inflammation [9].

PAP was first reported by Rosen et al. in 1958 [10], and for many years, the nature of this disorder was unknown and presented a variable natural history [11]. Major insights into PAP have been made in the past decade, and they have led to the notion that PAP is an autoimmune disorder. This has spurred new therapeutic approaches to this disorder. Until recently, there was no specific therapy for PAP and sequential WLL was the standard treatment.

Different pathologic conditions were also treated by WLL, but with variable success: cystic fibrosis [12–16], asthma, chronic obstructive lung disease, radioactive dust inhalation, alveolar microlithiasis, lipoid pneumonitis [17] or exogenous lipoid pneumonia [18–20], and silicosis [21–23].

Pulmonary Alveolar Proteinosis

Pathogenesis and Classification

Until recently, the pathogenesis of PAP was unknown. Most investigators have postulated a decreased clearance of surfactant from the alveolar space. Over the last decade, rapid progress was made towards the elucidation of the molecular mechanisms of PAP. Recent data suggest that GM-CSF has a pivotal role in PAP pathogenesis. GM-CSF is required for normal surfactant homeostasis. The disease is associated with neutralizing autoantibodies against GM-CSF. This new information allows the development of a new classification for this orphan lung disease and the use of new therapies. Some studies have been conducted with GM-CSF subcutaneous administration, and have obtained an overall response rate of 43%. The main conclusion is that GM-CSF appears to benefit a subset of patients with adult PAP, and may represent a novel alternative to the repeated WLLs in treatment of the disease [24].

Three forms of PAP are now recognized: primary, secondary, and congenital [9, 25, 26]. The primary (idiopathic) form of PAP is the most common disease presentation (more than 90% of all cases), its onset occurs in adulthood, and it has an autoimmune origin. It is associated with a high prevalence of circulating antiGM-CSF antibodies. Reduction of localized GM-CSF activity in the lung, secondary to the presence of neutralizing antiGM-CSF antibodies, decreases alveolar macrophage degradation, resulting in surfactant excess and accumulation [26]. There is no other associated underlying illness or exposure.

The secondary form also develops in adulthood, occurs with other conditions, and can be separated into two broad subgroups. These are systemic inflammatory disease or malignancy and specific exogenous exposure. Exposure to a high volume level of inorganic dusts (e.g., silica, aluminum, titanium, cement, wood), or fumes (chlorine, gas, gasoline, plastics) has been incriminated. Secondary PAP is likely related

to a relative deficiency of GM-CSF and related macrophage dysfunction [2–4, 6, 10, 27, 28].

The congenital form is often present in the neonatal period and results from a very rare gene mutation. This mutation is related to the surfactant receptor gene or to the GM-CSF gene. This form is rare, but is usually very severe. Neonatal respiratory distress syndrome is a presentation form of congenital PAP.

Clinical Manifestations

The patient presents dyspnea and hypoxemia, aggravated by exercise. Spontaneous remission can occur, but the therapeutic decision in PAP depends on the progression of the illness and the extent of the physiological impairment. The usual objective of WLL is the improvement in the clinical, physiological, and radiological aspects of the patient. The prognosis of PAP has greatly improved since the introduction of WLL by Ramirez-Riviera et al. in 1965.

Among adults, the typical age of presentation of the illness is 30–50 years. There is a male to female ratio of 2:1. The major symptom of PAP is a progressive dyspnea on exertion, spread over months and sometimes years. Dyspnea, the most common presenting symptom, is reported by approximately 55–80% of patients; however, approximately one-third of affected patients are asymptomatic, despite the infiltration in the alveolar air space. Nonproductive cough, fatigue, weight loss, and low-grade fever have also been described [11].

Radiographic Findings

Chest radiography is the most useful screening test, although very nonspecific [29, 30]. On chest radiography, bilateral symmetric alveolar opacities located centrally in mid and lower or upper lung zones are typical, yielding a “butterfly” distribution. High-resolution CT (HRCT) scanning reveals ground-glass opacification, predominantly in a homogeneous distribution. Thickened intralobular structures and interlobular septa in typical polygonal shapes may also be observed, referred to as “crazy-paving.” Crazy-paving is characteristic but not specific to PAP and can also be observed in patients with an acute respiratory distress syndrome, lipoid pneumonia, acute interstitial pneumonia, drug-related hypersensitivity reactions, and diffuse alveolar damage superimposed on usual interstitial pneumonitis [18].

Physiological Testing

Pulmonary function tests show a restrictive ventilatory defect with reduction in the total lung capacity and vital capacity. When present, the decrement in diffusing capacity for carbon dioxide (DLCO) is often out of proportion to the degree of the restrictive defect. Arterial blood gas analysis shows mild to moderate hypoxemia, with an elevated alveolar-arterial gradient and elevation in shunt fraction while breathing 100% O₂ [31].

Laboratory Investigation

BAL may help in establishing the diagnosis in clinically suspected cases. BAL fluid is opaque and presents a “milky” appearance, with large amounts of granular, acellular eosinophilic lipoproteinaceous material which is periodic acid Schiff (PAS) positive. Electron microscopic exam of BAL fluid can confirm the diagnosis [32, 33]. When allowed to stand, the fluid spontaneously separates into pale yellow, almost translucent supernatant and thick sediment.

Obtaining tissue for histopathology by open lung biopsy has been the “gold standard” for a long time. This biopsy performed by VATS is now unnecessary in the majority of cases of PAP. The combination of the clinical presentation, imaging findings, and BAL results are generally sufficient to make the diagnosis. Transbronchial biopsies may be occasionally used when needed. Surgical lung biopsy is sometimes necessary to make the diagnosis [9, 11, 34].

Furthermore, antiGM-CSF antibodies are increasingly used as a diagnostic tool in PAP. The quantitative assessment of antiGM-CSF antibodies in reference laboratories constitutes an important diagnostic and therapy-guiding measurement [35]. GM-CSF antibodies are present in all serum and BAL fluid samples from primary, idiopathic, PAP patients. BAL fluid levels of antiGM-CSF antibodies correlate better with the severity of PAP compared to serum titers [36]. Serial measurements of BAL or serum antiGM-CSF antibodies may be useful in monitoring disease activity and response to treatment [35, 37].

Therapy

The treatment depends on the form of PAP. In face of an idiopathic PAP, the use of WLL, GM-CSF, rituximab (Rituxan®) or plasmapheresis can be considered. For secondary PAP, treatment of the underlying condition or removal of the offending agent should be the first step to consider. When confronted with congenital PAP, WLL, supportive therapy or lung transplantation is the ultimate treatment.

Whole Lung Lavage

Treatment of idiopathic PAP has evolved from the use of a variety of nonspecific and largely ineffective agents, to the physical removal of the lipoproteinaceous material from the lungs (WLL), to the development of specific therapy targeting the underlying pathogenesis of the disorder. WLL has, for a long time, been considered the definitive therapy for PAP. The idea that the accumulated material could be physically removed from the lungs of PAP patients was first advanced in the early 1960s.

Specific indications for lung lavage include a definitive histological diagnosis and one of the following: resting $\text{PaO}_2 < 65 \text{ mmHg}$, alveolar-arterial O_2 gradient $\geq 40 \text{ mmHg}$, measured shunt fraction $> 10\text{--}12\%$, severe dyspnea and hypoxemia at rest or on exercise. It is critical not to perform WLL

when a patient has active bacterial pneumonia, since this can result in generalized sepsis and shock [26].

Although fairly well tolerated, WLL usually provides temporary symptomatic benefit, has to be repeated several times, requires prolonged general anesthesia, is complex to perform, is associated with potential morbidity, and fails to correct the primary defect in PAP. All these considerations make WLL a less-than-desirable treatment. Hence, the search for alternative modalities of therapy is still crucial [38].

Physical removal of the lipoproteinaceous material through repeated dilutions with saline solution is believed to be the mechanism from which WLL shows benefit, additional mechanisms including the bulk removal of antiGM-CSF antibody, as well as other possible immunologic effects on the effector cells, such as the alveolar macrophage or the type II epithelial cell, are possible [39].

Granulocyte Macrophage-Colony Stimulating Factor

Discovery of the alveolar macrophage involvement and antiGM-CSF neutralizing antibodies led to multiple trials examining the usefulness of GM-CSF therapy. Preliminary data suggest that about 50% of patients treated with GM-CSF experience improvement in pulmonary symptoms and function; however, the number of respondents appears to be less than with WLL. Given the experimental nature of GM-CSF therapy, the use of lung lavage is still the primary therapy in PAP [40].

Inhalation of nebulized GM-CSF has also been reported to improve lung function and facilitate clearance of the GM-CSF-antibody complexes from the lung. Additionally, a recent study utilizing a two-pronged approach showed a decrease in GM-CSF requirements by performing WLL followed by nebulization of GM-CSF. It also appears that high amounts of exogenous GM-CSF can overcome the endogenous neutralizing antibodies; especially if GM-CSF is directly administered to the lung. This result would seem to be explained by the lipoproteinaceous material cleared by WLL, and consequently inhaled GM-CSF could more readily reach the alveoli [26].

Although the positive effect of GM-CSF has been shown in idiopathic PAP, many important questions remain, including the optimal dose of GM-CSF, the optimal duration of treatment, the relation to the antiGM-CSF titers, and the optimal route of GM-CSF administration.

Other Therapies

Rituximab (Rituxan®) is a monoclonal antibody directed against B lymphocytes. Since 1997, rituximab has been demonstrated to be effective in various diseases mediated by autoantibodies, like in PAP [41]. Treatment with plasmapheresis, to decrease the level of Gm-CSF antibodies, has yielded mixed results [37]. Lung transplantation has been performed in patients whose health deteriorates despite WLL, but recurrence in the allograft has been reported [42].

Whole Lung Lavage Technique

In the author's institute [8], the team is composed of trained and experienced staff consisting of two anesthesia technicians (respiratory therapist), one nurse, two physiotherapists, and one anesthesiologist in charge of the anesthesia and the lung lavage.

Monitoring

WLL is performed under general anesthesia with basic monitoring, supplement respiratory monitoring, and sometimes invasive monitoring. In addition to the standard monitoring tools, an arterial cannulation is used for beat-to-beat measurement of blood pressure and for blood gases analysis. Some authors also suggest the use of continuous intra-arterial blood gases monitoring [43], pulmonary artery catheter, continuous monitoring of mixed venous oxygen saturation [44, 45], and transoesophageal echocardiography (TEE) [46, 47]. The pulmonary artery catheter may be used more as a therapeutic aid than a monitoring device by diverging blood flow away from the lavaged lung. TEE is sometimes useful to evaluate the cardiac function, mainly the right ventricle, in the presence of pulmonary hypertension.

The ventilator monitor found on most new anesthesia machines produces essential information during the WLL. The observation of the airway, pressure/volume loop (spirometry) on a breath-to-breath basis, is useful to detect any loss of lung isolation and to prevent flooding of the ventilated lung [8, 48].

General Anesthesia

Only light premedication with anxiolytic drugs is used. Pre-oxygenation is mandatory. General anesthesia is induced and maintained with intravenous agents, such as narcotics, benzodiazepine, intravenous anesthetic, and muscle relaxants. Inhaled anesthetic is very rarely used. After an initial 500 mL of crystalloid fluids, we rapidly switch to colloid fluid for an additional liter. The objective of this practice is to help recovery following accumulation of lavage liquid into the interstitial lung. Usually, the procedure for unilateral lavage lasts between 3–4 h and 5–6 h for a bilateral lavage. The use of a warming blanket over the legs helps to minimize heat loss as the thorax is completely denuded for the procedure.

Lung Separation

Lung separation is obtained by the use of a disposable left double-lumen tube. A left double-lumen tube with a carinal hook is used in our institution. The carinal hook offers a better stability of the tube given the numerous manipulations that occur during lung lavage. Adequate placement of the tube is visualized by fiberoptic bronchoscopy and air tightness is confirmed by a well-closed pressure–volume loop [7, 48]. Arterial blood gases are obtained during ventilation of both lungs simultaneously and then ventilating each lung

separately before and after the procedure to measure the effects of the WLL objectively. Prelavage evaluation determines which lung is the most impaired, mainly through imaging evaluations. Arterial blood gas analyses performed during an initial one-lung ventilation (OLV) trials on each side confirm the worst lung, which will be the first lung to have WLL.

Lung Lavage

The patient is kept in the supine position. To improve the effectiveness of the lavage, ventilation with FiO_2 1.0 is initiated for few minutes to denitrogenate both lungs [7]. OLV is instituted in the nonlavaged lung, which is the lung which provided the best oxygenation during the initial OLV trial. Confirmation of perfect lung isolation is obtained from the spirometry loop. A homemade disposable irrigation and drainage system (Fig. 35.1) is used to instill approximately 1 L of

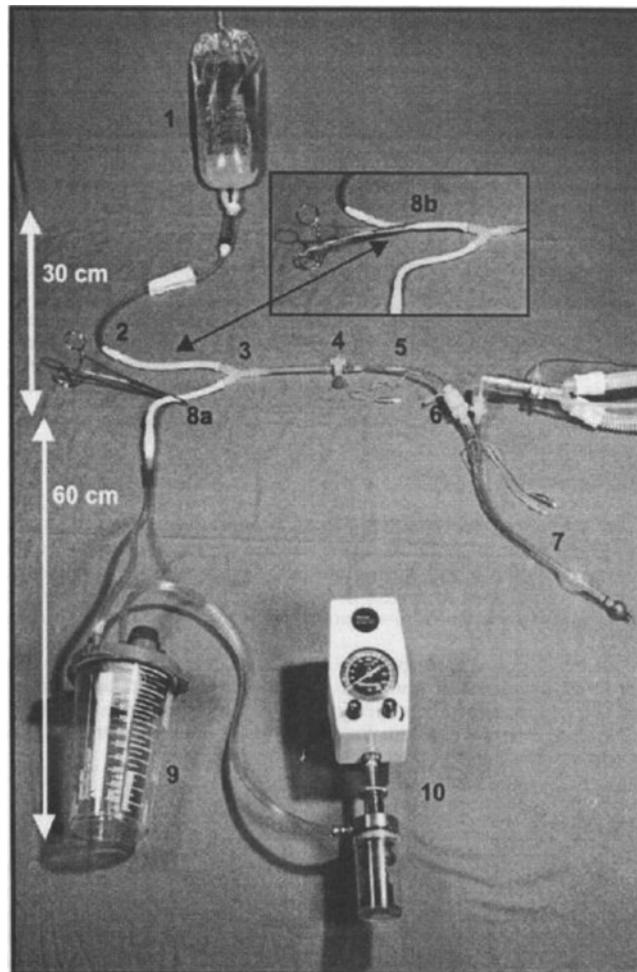


FIG. 35.1. Irrigation and drainage system. (1) Normal saline bag. (2) Large bore tubular set for bladder irrigation. (3) Y-adapter. (4) Three-way stop-cock for enteral feeding. (5a) Clamp on the drainage side tubing during instillation phase. (5b) Clamp on the instillation side tubing during drainage phase. (6) Vacuum bottle. (7) Suction unit. (8) 5 mm ID endotracheal tube, swivel adaptor, and double-lumen tube. (Reprinted from Bussières [8]. © 2001 with permission from Elsevier.).

warm normal saline (37°C). The irrigating liquid is suspended 30 cm above the patient's midchest level and the instillation takes approximately 5 min.

Mechanical maneuvers are used to increase the efficacy of the WLL. These techniques consist of manual chest physiotherapy, mainly percussions, vibrations, and pressure applied during the filling and the drainage phase [49, 50]. A flannel cloth is used to protect the patient's skin from irritation provoked by repetitive manipulations. Positional modifications are very useful to irrigate and to drain all the different segments of the lung. The full lateral position is used at least once during the procedure, usually at the fifth cycle. When the lavaged lung is up, extreme care must be taken to avoid the risk of leakage from this nondependant lavaged lung into the dependant and ventilated one.

A few minutes after the lung is completely filled with saline, it is rapidly drained into a container positioned 60 cm below the patient's midchest level, with the assistance of a small level of suction (<20 cm H₂O). This process is repeated ten times or more, as necessary, to obtain clear effluent lavage fluid. After six or seven cycles of lavage and drainage, manual ventilation of the lavaged lung is frequently used, half way during the drainage phase to help the evacuation of the alveolar material [51].

Over the past few years, the author has evaluated the amount of sediment recuperated following WLL for each lung separately. The sediment amount is determined after fluid lavages are allowed to stand for at least 2–3 h. At that time, the fluid spontaneously separates into a translucent supernatant and a thick sediment. The volume of sedimentation obtained allows quantifying the effect of WLL in each individual lung and patient. Strict in and out balance of lavage liquid must be recorded.

Bilateral Whole Lung Lavage

For more than 10 years, bilateral WLL during the same anesthetic period is now regularly performed with good results. When the effluent lavage fluid is clear on the first side WLL, the first stage of the procedure is over. Careful aspiration of the lavaged lung should be done, blindly with a suction catheter and also under direct vision with the use of a FOB.

In order to safely proceed with WLL of the contralateral lung, we proceed with a recuperation period for the recently lavaged lung. We ventilate both lungs with normal tidal volume (8–10 mL/kg) with addition of PEEP at a level varying from 7 to 12 cm H₂O for a period of 30–45 min. We administer furosemide (Lasix[®]) 10 mg to induce diuresis during this period and we entirely cover the patient's body to keep his/her temperature close to normal.

Following determination of the ability of the recently lavaged lung to support the OLV necessary for the lavage of the contralateral lung by serial blood gas sampling, we proceed with WLL of the second lung. Our goal is to obtain a OLV PaO₂ greater than 70 mmHg with a FiO₂ 1.0, with or without PEEP prior to beginning the second WLL. When we cannot

get satisfactory oxygenation, we use inhaled nitric oxide at 20 ppm or/and we insert a Swan-Ganz catheter under fluoroscopy in order to divert blood flow from the lavaged lung to the ventilated lung [23]. When the adequacy of oxygenation is demonstrated, the WLL on the second lung is performed similarly to the first one. If the blood gases are not adequate during OLV of the first lavaged lung prior to beginning the second stage, the procedure is aborted and a WLL of the remaining lung performed after a recovery period of 1–2 weeks.

Associated Broncho-Alveolar Lavage

In some specific cases, when the distribution of the alveolar infiltration is nonhomogeneous and is more localized in some specific lobes, the author adds to the standard WLL a series of BALs, directed to the main involved lobes. BAL is performed after the WLL, following the exchange from DLT to a large (>8 mm ID), single-lumen tube. A regular FOB is used to obtain a bigger suctioning channel. A BAL is performed at the segmental level. The injection of a maximum of 150 mL aliquots of normal saline, followed by a drainage period assisted by the same system as the one used during regular WLL. BAL are repeated as needed, that is, until the return of clear liquid from the treated lobe. Every involved lobe is done with the same technique. It seems to the author that this technique helps to perform a better WLL in certain cases.

Complications

The main complication is a decrease in arterial oxygen saturation [4], mainly during the drainage phase. Some liquid spillage from the lavaged lung to the nonlavaged lung may occur. Other complications such as pneumothorax and hydrothorax are rare, but may need to be drained, resulting in a postponed procedure. Postprocedure complications are pneumonia, sepsis, and rarely, respiratory distress syndrome [40].

Desaturation

Increase in the blood flow in the nonventilated lung occurs during the drainage phase (Fig. 35.2). This causes a decrease in arterial oxygen saturation [7]. The use of PEEP on the ventilated lung helps to improve oxygenation during the filling phase, but may worsen the PaO₂ during the drainage phase [52]. At that time, if needed (low SatO₂, i.e., <80% and/or for a prolonged period), a temporary partial unilateral pulmonary artery balloon occlusion with a pulmonary artery catheter, positioned under fluoroscopy in the artery of the lavaged lung, may be used. The occlusion diverts blood flow from the lavaged lung to the ventilated lung to improve oxygenation [53]. The use of nitric oxide with or without almitrine (Duxil[®]) infusion has been described [54]. Others have performed the WLL under hyperbaric conditions [55]. The use of an extracorporeal membrane oxygenator has been described to perform bilateral simultaneous WLL [56]. Recently, the use of a hyperoxygenated solution has been investigated. Its use

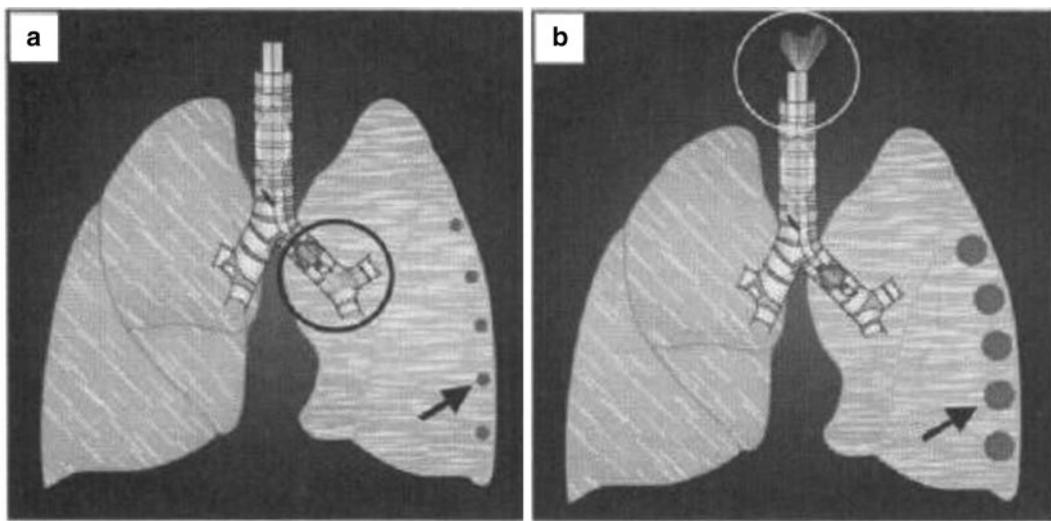


FIG. 35.2. *Desaturation*. (a) During the filling phase (circle), there is reduction of blood flow to the nonventilated lung, by compression of the pulmonary blood vessels (arrow). (b) During the drainage phase (circle), there is reperfusion of the nonventilated lung (arrow), creating a shunt, and leading to desaturation. (Reprinted from Bussières [8]. © 2001 with permission from Elsevier.).

improved oxygen supply in comparison to normal saline, as lavage solution, without obvious side effects [57].

Leakage

Spirometry must be used continuously to monitor and diagnose any air or liquid spillage from the lavaged lung. The mechanisms of liquid spillage differ depending on which side the lavaged lung is lying (Fig. 35.3). When the WLL is performed in the right lung with a left-sided DLT in place, overpressure comes from the trachea over the bronchial balloon. When leaking occurs, there is flooding of the left-ventilated lung. When it originates during a WLL performed on the left lung, leaking is caused by an overpressure in the left lung over the bronchial balloon or from a proximal displacement of the double-lumen tube (i.e., during lavage of the left lung the fluid tends to displace the DLT proximally).

If there is a modification of the spirometry loop, it is important to suspect flooding of the ventilated lung. At that time, it is essential to stop the irrigation, and to increase the drainage. Confirmation by fiberoptic bronchoscopy and treatment by vigorous suctioning and inflation of the involved lung should be performed. It is essential to assess the nonlavaged lung function before continuing the lavage to ensure that the flooded lung can provide adequate oxygenation during subsequent one lung ventilation. In the context of unilateral WLL, when flooding of the nonlavaged lung occurs, it frequently requires prolongation of ventilation during the postprocedure period to allow recovery [23]. Currently, with bilateral WLL, there is much less anxiety when this technique is performed during the same anesthesia period. The best treatment for this complication is prevention, which can be done with a secure fixation of

the double-lumen tube, the use of a double-lumen tube with a carinal hook, and by being careful not to dislodge the double-lumen tube during patient and head manipulations.

Termination of the Procedure

The end point that is clinically used to end a lung lavage is when the effluent lavage fluid is clear. Usually, between 10 and 15 L of saline are instilled into each lung (up to 50 L), and more than 90% of this volume is recovered, leaving a recuperation deficit of less than 10%. At the end of the procedure, the lavaged lung is thoroughly suctioned and the volume of the residual liquid aspirated is calculated in the “in and out” balance.

The effluent liquid of the WLL looks different depending on the pathology being treated. The sediment may seem milky following WLL for PAP (Fig. 35.4), while it may appear sandy if lung lavage is performed for silicosis. After reintubation with a single-lumen tracheal tube, a fiberoptic bronchoscopy control inspection is performed to look for the occurrence of undetected leakage throughout the procedure. During the fiberoptic bronchoscopy inspection, the author regularly observes local irritation of the distal tracheal mucosa, secondary to the movement of the double-lumen tube during WLL. The use of a double-lumen tube with a carinal hook has noticeably decreased the incidence of this irritation.

Conventional ventilation with PEEP is continued, usually for less than 2–4 h, to restore lung function in the recovery room. The patient is maintained sedated with propofol until gas exchange is adequate for weaning. Alveolar infiltrates seen on the chest X-ray immediately after WLL normally clear within 24–36 h (Fig. 35.5a–c). Observation in the ICU for 24 h is part of routine procedure.

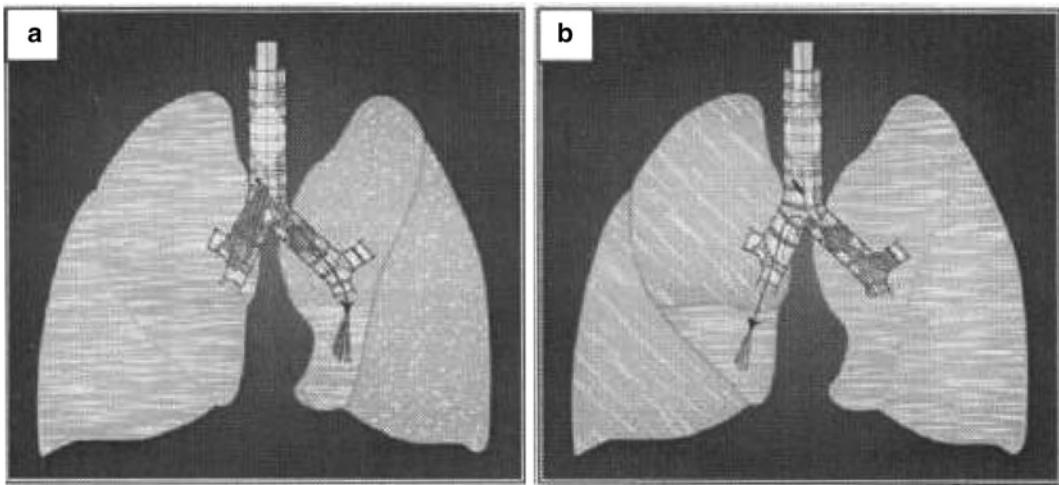


FIG. 35.3. *Leakage from lavage lung to the nonlavage lung.* (a) During right lung lavage, over pressure in the trachea provokes flooding in the left-ventilated lung. (b) During left lung lavage, over pressure in the left lung or displacement of the DLT provokes flooding of the right ventilated lung. (Reprinted from Bussières [8]. © 2001 with permission from Elsevier.).

FIG. 35.4. *Effluent from WLL.* Effluent from WLL in pulmonary alveolar proteinosis initially seems milky. When fluid lavages are allowed to stand for a few hours, thick sediment appears in the bottom of the collecting bottle. It is more abundant in the first bottles going to near zero in the last ones. (Reprinted from Bussières [8]. © 2001 with permission from Elsevier.).

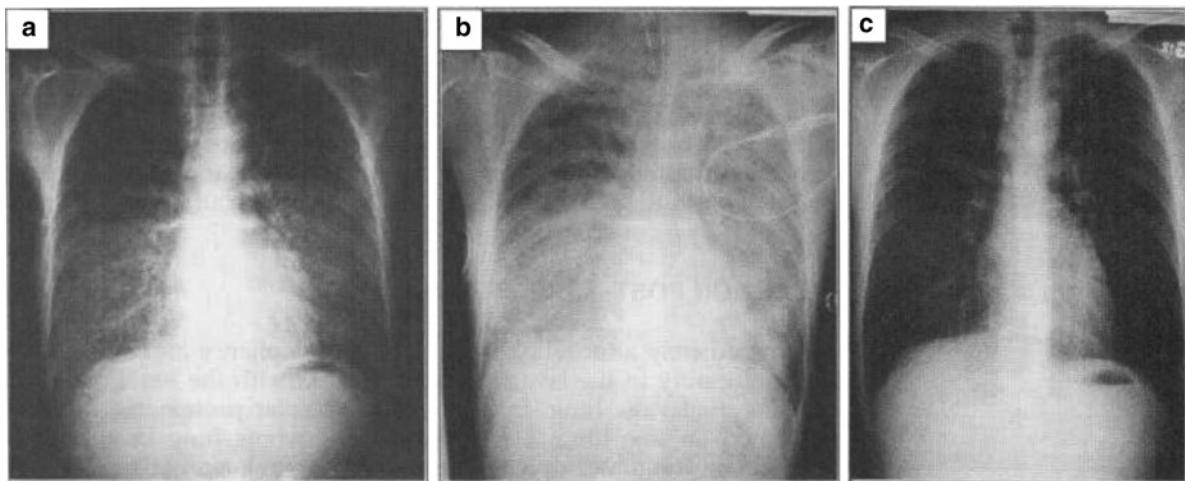
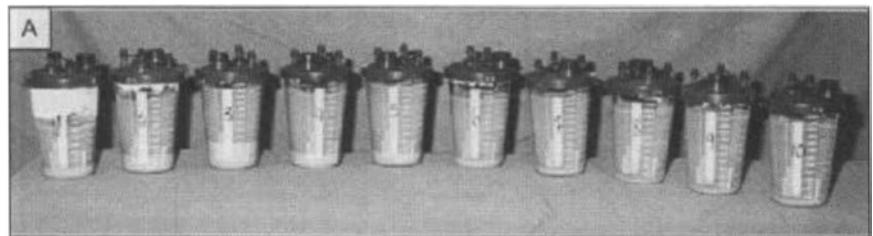


FIG. 35.5. *Radiological imaging.* (a) Before WLL alveolar infiltrates are more marked on the left side. (b) Immediately after left WLL, note the important alveolar edema resulting from the procedure. (c) Three days after the right side WLL, note the important amelioration of the two lungs. (Reprinted from Bussières [8]. Anesthesiology Clinics of North America. © 2001 with permission from Elsevier.).

Postwhole Lung Lavage Evolution

Before bilateral WLL performed in the same anesthetic episode, WLL was usually performed on the sickest lung; then at least a week later, WLL of the contra-lateral lung was completed. At that time, oxygenation was usually not a problem because the treated and now near-normal lung was used to support gas exchange during the second procedure. We realized, with the experience of bilateral WLL, that the lung recuperated rapidly enough to allow the contralateral WLL in less than an hour after the initial one.

The impact of WLL on the natural history of idiopathic PAP is difficult to ascertain, given the absence of randomized prospective trials or large, long-standing registries. Since its introduction into practice, therapeutic WLL has largely remained anecdotal as an art rather than a science. However, practitioners of this procedure widely believe that patients with PAP improve symptomatically as well as by gas exchange criteria with a WLL. It should be noted that congenital PAP appears to be particularly unlikely to respond to WLL [9]. After WLL, patients usually have marked subjective improvement that correlates with increases in PaO_2 (at rest and exercise), vital capacity, diffusing capacity, and clearing of the chest roentgenogram (Fig. 35.5) or CT scan (Fig. 35.6). Some patients require lavage every few months, whereas others remain in remission for several years. The disease may eventually show late recurrence. In PAP, WLL is proven to be successful because the lavage removes enormous accumulations of alveolar lipoproteinaceous material, but also probably because it interrupts the pathogenic loop, decreasing the level of antiGM-GSF at the alveolar site, and temporarily restores the activity and function of the macrophages.

An excellent retrospective review of all published articles, describing over 400 separate individual cases of PAP, was published in 2002 by Seymour and Presneill [9]. They reported 41 patients with prelavage and postlavage paired gas exchange results, the PaO_2 improved by 20 mmHg, breathing room air, within 3 months following WLL. The improvement in other pulmonary function parameters or diffusing capacity was less impressive. Their results also indicate that the median

total number of lavages performed was two and that the median symptom-free period after one session of WLL was 15 months.

With regard to survival, in their analysis of the literature, Seymour and Presneill indicate that the overall survival at 5 years from the time of diagnosis is higher for patients who underwent therapeutic lung lavage during the course of their disease (94 vs. 85%, for those not lavaged). This was based on a series of 146 patients who were lavaged and 85 patients who were not [9].

Pediatric Whole Lung Lavage

WLL has been used in the pediatric and neonatal population with some success. WLL is technically difficult in infants and small children because of the incapacity to ventilate part of the lung or one lung safely and adequately during lavage of other areas or other lung.

Small double-lumen tubes (Bronchopart®, size 26, 28 and 32, Willy Rusch AG, 71394 Kernen, Germany or Broncho-Cath® size 28 and 32, Mallinckrodt Medical, Athlone, Ireland) are now available for use in children over 8–10 years old or weighing over 30 kg. Small FOBs are also available to verify and adjust the final position of this double-lumen tube. When the airway of a child accepts a double-lumen tube, the WLL technique is similar to of the one performed in adults.

If the airway is too small to insert a double-lumen tube, WLL is technically more challenging. Different methods to isolate both lungs have been described [19, 58, 59]. Recently, a publication described the use of two side-by-side cuffed tubes (one tracheal 3.0 mm and one bronchial 3.5 mm) in a 11 kg child for unilateral WLL [60]. Airway isolation has been obtained for an infant as small as 2 kg [59]. When the perfect isolation of both lungs is obtained, WLL is performed, as with a double-lumen tube in place, but with much more attention to the stability of the airway devices.

When techniques described above cannot be applied, mainly in patients weighing less than 10 kg, ECMO can be used to oxygenate the patient while bilateral simultaneous

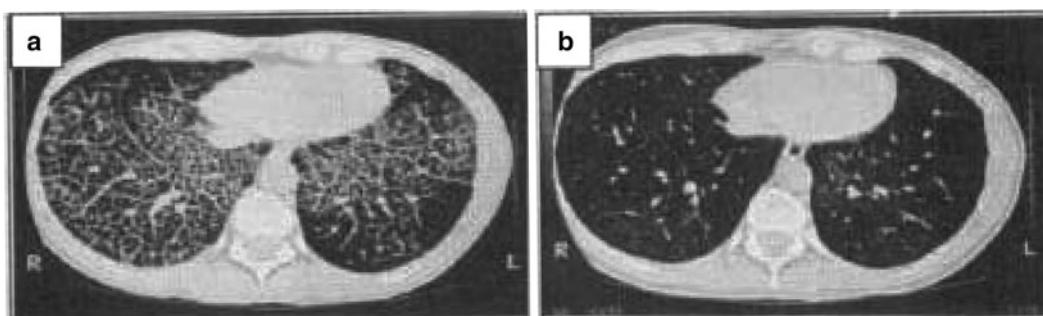


FIG. 35.6. Radiological imaging. (a) Chest CT scan before WLL, note the important amount of alveolar material looking like "crazy-paving." (b) CT scan 3 days after WLL, the alveolar material has been cleared out. (Reprinted from Bussières [8]. © 2001 with permission from Elsevier.).

WLL is performed. Different approaches for the vascular cannulation have been described [61, 62]. Finally, one case report describes the use of partial liquid ventilation with perflubron (LiquidVent®; Alliance Pharmaceuticals Corp. and Hoechst Marion Roussel) for 4 days following WLL done under ECMO in a 3.4 kg infant aged 6 weeks [63].

Conclusion

After more than 40 years of evolution, WLL is an efficient and safe technique. This technique is now frequently performed as a bilateral procedure during the same anesthetic. This procedure can be adapted to a large variety of patients and diseases. When WLL does not lead to any beneficial effect to the patient, there are now new modalities that can be combined to WLL.

Clinical Case Discussion

A 47-year-old woman was referred to our team for WLL 4 years ago. At that time, she had presented symptoms, mainly increasing dyspnea, for 6 months. An open lung biopsy had

been performed at her hospital to establish the diagnosis of PAP. Pulmonary function tests performed in our institute showed a mild restrictive syndrome, a DLCO 58% predicted and a PaO_2 of 68 mmHg. Radiological investigation revealed a homogeneous distribution with the involvement of bilateral superior lobes, middle lobe and bilateral supero-dorsal segment of the inferior lobe. A BAL confirmed the diagnosis of PAP.

A first bilateral WLL was performed and moderately effective results were obtained. During the next two and a half years period, the patient underwent six bilateral WLL, at intervals varying between 4 and 12 months, without improvement in the clinical status, laboratory results or radiological imaging.

During the last WLL, BAL was also performed as the radiological infiltrations were localized mainly in the left superior lobe, and the supero-dorsal segment of the bilateral inferior lobes (Fig. 35.7a–c).

Nine months later, the patient complained about the same symptoms without marked improvement following any of the performed WLL. The serum level of antiGM-CSF antibodies was measured, and the result, 203 $\mu\text{g}/\text{mL}$ (normal $<3 \mu\text{g}/\text{mL}$), confirmed the diagnosis of primary PAP. In the following months, the patient received GM-CSF, but this treatment was discontinued because of lack of improvement and side effects.

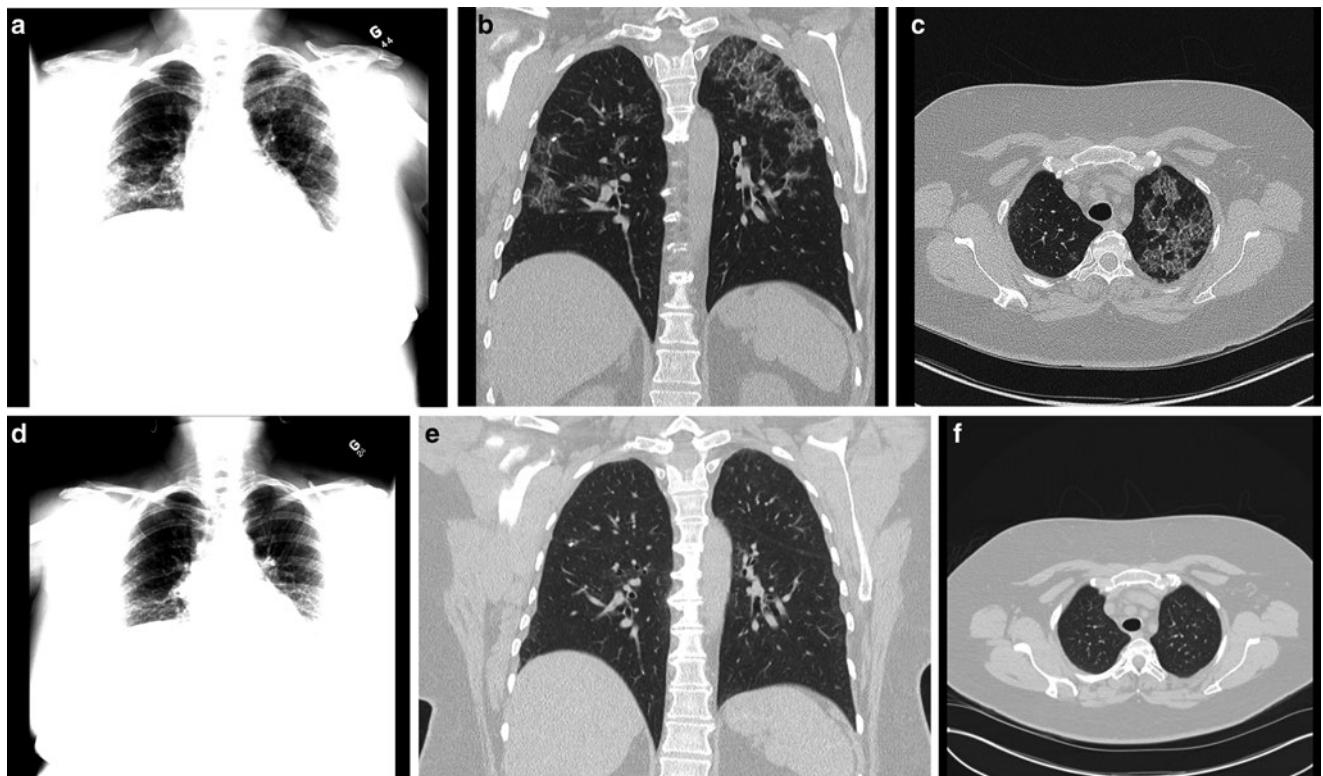


FIG. 35.7. Radiological imaging of pulmonary alveolar proteinosis. (a) Antero-posterior view demonstrating the heterogeneous radiological infiltrations. They are mainly localized in the left superior lobe, and the supero-dorsal segment of the bilateral inferior lobes. (b) High definition computed tomography scan, coronal plane, showing the same involvement. (c) High definition computed tomography scan, axial plane, showing crazy paving imaging in the left upper lobe. (d) Antero-posterior view demonstrating the disappearance of the radiological infiltrations. (e) High definition computed tomography scan, coronal plane, showing the same improvement. (f) High definition computed tomography scan, axial plane, showing that the alveolar material has cleared out.

A few months later, the patient was placed on rituximab (Rituxan®), but this was also discontinued after a few cycles since there was clinical and radiological deterioration.

How Would You Manage This Patient?

Given this situation, we performed a new WLL, associated with specific BAL. The sediment recuperation was increased following the BAL. In the following days after the recovery from the WLL, we began GM-CSF by inhalation, once daily.

At 1 and 3 months follow-up, the patient presented a significant improvement of her clinical status, for the first time since the first WLL. The radiologic image completely cleared (Fig. 35.7d-f) with this associated therapy, but the laboratory investigations remained unchanged.

We decreased GM-CSF inhalations and ceased it completely after three months. Four months later her pulmonary function testing were better and more than a year later she is always completely asymptomatic. This case report promotes the usefulness of multiple therapies that should be carried out to efficiently treat patients suffering from PAP.

References

1. Vincente G. Le lavage des poumons. *Presse Médicale*. 1929; 1266.
2. Ramirez-Riviera J. The strange beginnings of diagnostic and therapeutic bronchoalveolar lavage. *P R Health Sci J*. 1992;11(1):27.
3. Ramirez-Riviera J, Kieffer Jr RF, Ball Jr WC. Bronchopulmonary lavage in man. *Ann Intern Med*. 1965;63(5):819–28.
4. Ramirez-Riviera J. Bronchopulmonary lavage. New techniques and observations. *Dis Chest*. 1966;50(6):581–8.
5. Ramirez-Riviera J, Schultz RB, Dutton RE. Pulmonary alveolar proteinosis: a new technique and rationale for treatment. *Arch Intern Med*. 1963;112:419–31.
6. Spragg RG, Benumof JL, Alfery DD. New methods for the performance of unilateral lung lavage. *Anesthesiology*. 1982;57(6): 535–8.
7. Benumof JL. Anesthesia for special elective therapeutic procedures. In: Benumof JL, editor. *Anesthesia for thoracic surgery*. Philadelphia: WB Saunders. 1994.
8. Bussières JS. Whole lung lavage. *Anesthesiol Clin N Am*. 2001;19(3):543–58.
9. Seymour JF, Presneill JJ. Pulmonary alveolar proteinosis: progress in the first 44 years. *Am J Respir Crit Care Med*. 2002;166(2):215–35.
10. Rosen SH, Castleman B, Liebow AA. Pulmonary alveolar proteinosis. *N Engl J Med*. 1958;258(23):1123–42.
11. Goldstein LS et al. Pulmonary alveolar proteinosis: clinical features and outcomes. *Chest*. 1998;114(5):1357–62.
12. Braunstein MS, Fleegler B. Failure of bronchopulmonary lavage in cystic fibrosis. *Chest*. 1974;66(1):96–9.
13. Lober CW, Saltzman HA, Kylstra JA. Volume-controlled lung lavage in a woman with cystic fibrosis. *Chest*. 1975;68(3):382–3.
14. Dahm LS et al. Comparison of three techniques of lung lavage in patients with cystic fibrosis. *Chest*. 1977;72(5):593–6.
15. Spock A. State of the art of lung lavage in patients with cystic fibrosis. In: International conference of cystic fibrosis. 1977.
16. Adkins MO, Chan JC, Brodsky JB. Unsuccessful unilateral bronchopulmonary lavage for a patient with severe cystic fibrosis. *J Cardiothorac Anesth*. 1989;3(4):481–5.
17. Chang HY et al. Successful treatment of diffuse lipid pneumonia with whole lung lavage. *Thorax*. 1993;48(9):947–8.
18. Wong CA, Wilsher ML. Treatment of exogenous lipid pneumonia by whole lung lavage. *Aust N Z J Med*. 1994;24(6):734–5.
19. Ciravegna B et al. Mineral oil lipid pneumonia in a child with anoxic encephalopathy: treatment by whole lung lavage. *Pediatr Pulmonol*. 1997;23(3):233–7.
20. Danel C et al. Therapeutic applications of bronchoalveolar lavage. *Eur Respir J*. 1992;5(10):1173–5.
21. Mason GR et al. Treatment of mixed-dust pneumoconiosis with whole lung lavage. *Am Rev Respir Dis*. 1982;126(6):1102–7.
22. Wilt JL et al. Reduction of lung dust burden in pneumoconiosis by whole-lung lavage. *J Occup Environ Med*. 1996;38(6):619–24.
23. Bussières J et al. Feasibility, safety and efficacy of whole-lung lavage in silicosis. *Can J Anesth*. 1999;46(5):A43.
24. Seymour JF et al. Therapeutic efficacy of granulocyte-macrophage colony-stimulating factor in patients with idiopathic acquired alveolar proteinosis. *Am J Respir Crit Care Med*. 2001;163(2):524–31.
25. Chan ED, Talmadge EK. Clinical manifestations and etiology of pulmonary alveolar proteinosis in adults. *UpToDate* 2010, March 12.
26. Huizar I, Kavuru MS. Alveolar proteinosis syndrome: pathogenesis, diagnosis, and management. *Curr Opin Pulm Med*. 2009;15(5):491–8.
27. Rodi G et al. Whole lung lavage. *Monaldi Arch Chest Dis*. 1995;50(1):64–6.
28. Persson A. Pulmonary alveolar proteinosis. In: Fishman A, editor. *Fishman's pulmonary diseases and disorders*. New York: McGraw-Hill; 1998.
29. Lee K et al. Pulmonary alveolar proteinosis: high-resolution CT, chest radiographic, and functional correlations. *Chest*. 1997;111:989–95.
30. Arcasoy SM, Lanken PN. Images in clinical medicine. Pulmonary alveolar proteinosis. *N Engl J Med*. 2002;347(26):2133.
31. Martin RJ, Rogers RM, Myers NM. Pulmonary alveolar proteinosis: shunt fraction and lactic acid dehydrogenase concentration as aids to diagnosis. *Am Rev Respir Dis*. 1978;117(6):1059–62.
32. Costello JF et al. Diagnosis and management of alveolar proteinosis: the role of electron microscopy. *Thorax*. 1975;30(2):121–32.
33. Gilmore LB, Talley FA, Hook GE. Classification and morphometric quantitation of insoluble materials from the lungs of patients with alveolar proteinosis. *Am J Pathol*. 1988;133(2):252–64.
34. Rubinstein I, Mullen JB, Hoffstein V. Morphologic diagnosis of idiopathic pulmonary alveolar lipoproteinosis-revisited. *Arch Intern Med*. 1988;148(4):813–6.
35. Bonfield TL, Kavuru MS, Thomassen MJ. Anti-GM-CSF titer predicts response to GM-CSF therapy in pulmonary alveolar proteinosis. *Clin Immunol*. 2002;105(3):342–50.
36. Lin FC et al. Clinical significance of anti-GM-CSF antibodies in idiopathic pulmonary alveolar proteinosis. *Thorax*. 2006;61(6): 528–34.
37. Luisetti M et al. Plasmapheresis for treatment of pulmonary alveolar proteinosis. *Eur Respir J*. 2009;33(5):1220–2.
38. Ioachimescu OC, Kavuru MS. Pulmonary alveolar proteinosis. *Chron Respir Dis*. 2006;3(3):149–59.
39. Kavuru MS, Popovich M. Therapeutic whole lung lavage: a stop-gap therapy for alveolar proteinosis. *Chest*. 2002;122(4):1123–4.

40. Chan ED, Talmadge EK. Diagnosis and treatment of pulmonary alveolar proteinosis in adults. UpToDate 2010, November 12.
41. Borie R et al. Rituximab therapy in autoimmune pulmonary alveolar proteinosis. *Eur Respir J.* 2009;33(6):1503–6.
42. Parker LA, Novotny D. Recurrent alveolar proteinosis following double lung transplantation. *Chest.* 1997;111:1457.
43. Takahashi S et al. [Continuous intra-arterial blood gas monitoring during bronchopulmonary lavage for pulmonary alveolar proteinosis]. *Masui.* 1998;47(5):626–31.
44. Loubser PG. Validity of pulmonary artery catheter-derived hemodynamic information during bronchopulmonary lavage. *J Cardiothorac Vasc Anesth.* 1997;11(7):885–8.
45. Cohen E, Eisenkraft JB. Bronchopulmonary lavage: effects on oxygenation and hemodynamics. *J Cardiothorac Anesth.* 1990;4(5):609–15.
46. McMahon CC, Irvine T, Conacher ID. Transoesophageal echocardiography in the management of whole lung lavage. *Br J Anaesth.* 1998;81(2):262–4.
47. Swenson JD, Astle KL, Bailey PL. Reduction in left ventricular filling during bronchopulmonary lavage demonstrated by transesophageal echocardiography. *Anesth Analg.* 1995;81(3):634–7.
48. Bardoczky GI, Engelman E, d'Hollander A. Continuous spirometry: an aid to monitoring ventilation during operation. *Br J Anaesth.* 1993;71(5):747–51.
49. Hammon WE, McCaffree DR, Cucchiara AJ. A comparison of manual to mechanical chest percussion for clearance of alveolar material in patients with pulmonary alveolar proteinosis (phospholipidosis). *Chest.* 1993;103(5):1409–12.
50. Bracci L. Role of physical therapy in management of pulmonary alveolar proteinosis. A case report. *Phys Ther.* 1988;68(5):686–9.
51. Bingisser R et al. Whole-lung lavage in alveolar proteinosis by a modified lavage technique. *Chest.* 1998;113(6):1718–9.
52. Julien T et al. [Effect of positive end expiratory pressure on arterial oxygenation during bronchoalveolar lavage for proteinosis]. *Ann Fr Anesth Rèanim.* 1986;5(2):173–6.
53. Nadeau MJ, Cote D, Bussieres J.S. The combination of inhaled nitric oxide and pulmonary artery balloon inflation improves oxygenation during whole-lung lavage. *Anesth Analg.* 2004;99(3):676–9, table of contents.
54. Moutafis M et al. Improving oxygenation during bronchopulmonary lavage using nitric oxide inhalation and almitrine infusion. *Anesth Analg.* 1999;89(2):302–4.
55. Biervliet J et al. Whole-lung lavage under hyperbaric conditions. In: Erdmann W, editor. *Oxygen transport to tissue XIV.* New York: Plenum. 1992.
56. Cohen ES, Elpern E, Silver MR. Pulmonary alveolar proteinosis causing severe hypoxic respiratory failure treated with sequential whole-lung lavage utilizing venous extracorporeal membrane oxygenation: a case report and review. *Chest.* 2001;120(3):1024–6.
57. Zhou B et al. Hyperoxygenated solution for improved oxygen supply in patients undergoing lung lavage for pulmonary alveolar proteinosis. *Chin Med J (Engl).* 2009;122(15):1780–3.
58. McKenzie B, Wood RE, Bailey A. Airway management for unilateral lung lavage in children. *Anesthesiology.* 1989;70(3):550–3.
59. Moazam F et al. Total lung lavage for pulmonary alveolar proteinosis in an infant without the use of cardiopulmonary bypass. *J Pediatr Surg.* 1985;20(4):398–401.
60. Paquet C, Karsli C. Technique of lung isolation for whole lung lavage in a child with pulmonary alveolar proteinosis. *Anesthesiology.* 2009;110(1):190–2.
61. Hiratzka LF et al. Bilateral simultaneous lung lavage utilizing membrane oxygenator for pulmonary alveolar proteinosis in an 8-month-old infant. *Ann Thorac Surg.* 1983;35(3):313–7.
62. Lippmann M, Mok MS, Wasserman K. Anaesthetic management for children with alveolar proteinosis using extracorporeal circulation. Report of two cases. *Br J Anaesth.* 1977;49(2):173–7.
63. Tsai WC et al. Liquid ventilation in an infant with pulmonary alveolar proteinosis. *Pediatr Pulmonol.* 1998;26(4):283–6.

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Key Points

- Lung volume reduction surgery (LVRS) is a viable option for a select group of emphysema patients.
- Effective preoperative pulmonary rehabilitation and careful patient selection criteria promote favorable outcomes.
- Effective perioperative pain management and early extubation are significant factors that minimize postoperative complications and lead to better outcome.
- LVRS improves dyspnea, exercise tolerance, and increases potential for patient survival in appropriately selected patients.

Introduction

Approximately 13.5 million persons in the United States are afflicted with COPD, and 3.1 million of these patients have emphysema [1]. Airflow obstruction associated with chronic bronchitis or emphysema occurs due to a loss of the elastic recoil properties of the lung and chest wall and the collapse of small airways, creating a permanent state of hyperinflation. The anterior-posterior diameter of the chest wall is markedly expanded and the diaphragm is flattened leading to progressive dyspnea and a gradual increase in the work of breathing. As the disease progresses, patients become increasingly debilitated, require supplemental oxygen, and display poor exercise tolerance. Lung volume reduction surgery (LVRS) offers a select group of patients the possibility of improved exercise

tolerance, reduction in dyspnea, improved quality of life, and an extended life span. It has been suggested that LVRS may provide these patients with a benefit that otherwise cannot be achieved by any means other than lung transplantation.

More recently, less invasive bronchoscopic procedures have been used to achieve the same goals as LVRS. Bronchial blockers, bronchial valves, and biologic glue have been used in an attempt to provide lung reduction with an acceptable risk profile in patients with advanced heterogenous emphysema. This technique could provide palliation to patients who are currently not considered for LVRS.

History of Lung Volume Reduction Surgery (LVRS)

In 1957, Otto Brantigan, M.D., described a surgical technique for patients with end-stage emphysema that was designed to alleviate symptoms of severe dyspnea and exercise intolerance [2]. It was Brantigan's intent to remove functionally useless areas of the lung in order to restore pulmonary elastic recoil, thus increasing the outward traction on small airways and subsequently improve airflow. Brantigan believed that this technique could restore diaphragmatic and thoracic contours that would improve respiratory excursion. Additionally, he reasoned that by excising the nonfunctional lung tissue, the compressive effects exerted on normal lung tissue could be relieved and result in improved V/Q matching. Unfortunately, the operative mortality was significant and no objective

measures of benefit could be documented. Thus, early LVRS was abandoned as a viable therapy for patients with end-stage emphysema until 1993.

In 1996, Joel Cooper, M.D., authored an editorial advocating the technique of LVRS as a “logical, physiologically sound procedure of demonstrable benefit for a selected group of patients with no alternative therapy” [3]. He further stated that the successful application of LVRS was “made possible through an improved understanding of pulmonary physiology, improved anesthetic and surgical techniques, and lessons learned from experience with lung transplantation.” Although Dr. Cooper touted the benefits of LVRS for certain patients, he did not minimize the surgical risk and suggested that this was not a procedure to be performed in all health care centers across the country. He made the following proposal: (1) health care providers should restrict the application of this (LVRS) procedure to a limited number of centers of excellence; (2) such centers should be required to document and report specified information regarding morbidity, mortality, and objective measures of outcome; and (3) these data should be periodically reviewed and evaluated by a scientific panel before approval to continue performing the procedure is approved. Additionally, he advocated that the patients who would otherwise qualify for lung transplantation should be simultaneously evaluated for LVRS so that they would receive the procedure proving to be most appropriate. LVRS was considered to be a palliative procedure to reduce dyspnea, improve exercise tolerance and the quality of daily life. Most of Dr. Cooper’s patients achieved these goals as well as an improvement in airflow, a reduction of lung hyperinflation and improved alveolar gas exchange.

Shortly after Dr. Cooper’s report regarding the success of LVRS was published, there was a widespread application of the technique. Analysis of the outcome data for Medicare patients revealed a 23% mortality rate at 12 months following LVRS prompting the discontinuation of funding for this procedure in 1996 due to the associated high risks and costs [4]. Subsequently, the National Heart, Blood and Lung Institutes designed a prospective, randomized clinical trial, the National Emphysema Treatment Trial (NETT), that evaluated the efficacy and safety of LVRS plus medical therapy vs. medical therapy alone [5].

Clinical Features of Emphysema

Emphysema is usually the end result of cigarette smoking, but can also be caused by alpha-1-antitrypsin deficiency [6, 7]. It is a chronic progressive disorder that ultimately leads to disability and early death. The cardinal physiologic defect in emphysema is a decrease in elastic recoil of the lung tissue that results in the principal physiologic abnormalities of decreased maximum expiratory airflow, leading to air trapping and hyperinflation and severely limited exercise capacity [7, 8].

Areas of severely emphysematous lung constitute dead space and result in compression of the adjacent lung tissue rendering it less capable of exerting the better-preserved elastic recoil on its adjoining airways. This leads to an increase in airway resistance and a reduction of expiratory airflow due to decreases in the driving and transmural pressures that maintain the patency of intra-parenchymal airways.

The distribution of emphysema in the lung parenchyma adversely affects alveolar gas exchange compounded by an increase in ventilatory drive, premature initiation of inspiration, hyperinflation and positive alveolar pressure at end expiration (auto-PEEP). As the disease progresses, inspiration becomes more difficult as a more negative inspiratory pressure is required to counteract auto-PEEP. Hyperinflation of the lungs leads to remodeling of the chest wall via progressive flattening of the diaphragm and alterations in the anterior-posterior diameter of the rib cage. These changes contribute directly to the increased work of breathing associated with emphysema [9].

Preoperative Medical Management of Emphysema Patients

The American Thoracic Society established guidelines for the diagnosis and management of emphysema [10]. Patients who are evaluated and considered for LVRS may remain symptomatic despite optimal medical management. Prior to LVRS, a structured pulmonary rehabilitation program is instituted with the goals of halting the progressive decline in lung function, preventing exacerbations of the disease, improving exercise capacity and quality of life, and prolonging survival. This is achieved through exercise training, optimization of medical therapy, patient education, psychosocial evaluation, and nutritional counseling and management.

The only treatment that has been shown to alter the rate of progression of COPD is cessation of smoking [11]. The majority of programs will require cessation of smoking for at least 6 months prior to considering the patient as a surgical candidate for LVRS.

Patients with severe emphysema are usually severely dyspneic even during minimal physical activity and as a result, they become sedentary leading to progressive exercise deconditioning. For this reason, exercise training is an essential component for the preoperative preparation of the patient undergoing LVRS. The optimal training program is supervised by a specialized nurse and physician and lasts for at least 6 weeks prior surgery. Training consists of walking for a distance on a flat surface, bicycle ergometer training, and weight lifting. These exercises are combined with a special diet. There are several advantages of an exercise program prior to surgery: (a) the patient’s willingness to cooperate can be assessed, (b) endurance and exercise tolerance is increased, which will be helpful for early mobilization after surgery [12],

and (c) maximal oxygen consumption can be increased in many subjects [13].

Influenza immunization and pneumococcal vaccination are recommended for the prevention of life-threatening infection [10]. Exacerbations of bronchospasm and infection are treated with steroids and antibiotics, respectively [14, 15]. Furthermore, beta-adrenergic agonists such as theophylline and anticholinergics are recommended for treatment of COPD and asthma [10]. Although these interventions are believed to shorten the duration of individual episodes and to minimize symptoms, there is little evidence that they either alter the natural history of the disease or reduce mortality. Bronchodilators improve lung function, exercise capacity, and quality of life in patients with COPD but are of limited benefit to patients without reversible airway disease [10].

Long-term home oxygen therapy in chronically hypoxic patients is the only treatment for COPD that has been documented to decrease mortality rates [16, 17]. Adjunctive forms of therapy, such as the use of mucolytics to control respiratory secretions or narcotics to reduce the sensation of dyspnea, have been used in selected COPD patients [10]. In end-stage COPD patients, single or double lung transplantation has been used as a last resort, but this option is limited by financial resources and the number of donor organs.

Patients presenting for LVRS are frequently very anxious secondary to the dyspnea and asthmatic crises they experienced in the past. Psychological factors can induce an asthma attack that is a dangerous complication during the perioperative period. Anxiety is associated with an increase in respiratory frequency leading to an increase in dynamic pulmonary hyperinflation and dyspnea [18]. Therefore, it is important that the anesthesiologist is able to establish a good relationship with the patient before surgery. The optimal psychological preconditions are likely to be achieved when the preoperative preparation, preoperative visit, insertion of a thoracic epidural catheter, administration of general anesthesia, and early postoperative therapy are conducted by the same physician or a team well known to the patient. Anxiolytic therapy may be necessary during the preoperative and perioperative period.

Evaluation of Patients for LVRS and Selection Criteria

General Evaluation

General criteria for patient selection and recommendations for screening procedures are described by Weinmann and Hyatt [19]. These selection criteria may vary between institutions. Distinct selection criteria for LVRS candidates were published by Daniel et al. [20] and are shown in Table 36.1.

Whether patients with significant hypercapnia should undergo LVRS is controversial [19, 21]. Furthermore, some institutions report significant coronary artery disease (coronary

TABLE 36.1. General inclusion criteria for LVRS.

- Diagnosis of COPD
- Patient history, physical examination, lung function test, chest X-ray, etc.
- Smoking cessation for greater than 1 month
- Age <75 years
- FEV₁ between 15 and 35% of predicted
- P_aCO₂ <55 mmHg
- Prednisone requirement <20 mg/day
- PAP_{sys} <50 mmHg
- No previous thoracotomy or pleurodesis
- Absence of symptomatic coronary artery disease
- Absence of chronic asthma or bronchitis
- Commitment to preop and postop supervised pulmonary rehabilitation for 6 weeks

COPD chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in one second; P_aCO₂, arterial carbon dioxide pressure in mmHg; PAP_{sys}, systolic pulmonary arterial pressure in mmHg

Reprinted from Daniel et al. [20] with permission from Wolters Kluwer Health

artery stenosis >70%) diagnosed in 15% of their asymptomatic LVRS candidates and thus, they recommend left and right heart cardiac catheterization preoperatively [22]. This invasive cardiac screening seems justified by several case reports of myocardial infarction during and after LVRS. Other institutions recommend limiting cardiac screening to transthoracic echocardiography [19]. In general, it is reasonable for centers with less experience to employ strict criteria for patient selection to minimize patient morbidity and mortality.

Anatomic/Radiologic Evaluation

The chest X-ray should provide evidence of hyperinflated lungs, large intercostal spaces, retrosternal airspace, flattened diaphragm, and high transparency of the lungs (see Fig. 36.1a). For a precise morphologic evaluation, a high-resolution computer tomography (HR-CT) of the chest is essential for identification of nonhomogeneous areas within the lungs. HR-CT locates the target areas for resection. An ideal anatomical precondition for LVRS is marked inhomogeneity of the lung structure, where normal lung tissue and severely destroyed, over-distended tissue are present in the same lung (see Fig. 36.2a). Homogeneous distribution of the disease proved to be an unfavorable precondition (see Fig. 36.2b).

Several authors have demonstrated that patients presenting with severe inhomogeneity are very likely to benefit from LVRS [23–25]. Two reasons might account for this: (1) compressed, normal lung tissue is released after removing adjoining hyperinflated, nonfunctional, destroyed tissue, and thus, the pulmonary mechanics of the remaining tissue are improved; and (2) surgery is easier to perform if the target areas are clearly visible. In many centers, lung perfusion scintigraphy is still routinely performed for screening LVRS candidates primarily to rule out ventilation–perfusion mismatch. However, chest computed tomography has been shown to

FIG. 36.1. A lateral chest X-ray is shown. (a) Depicts the patient before lung volume reduction surgery (LVRS): the thorax is barrel-shaped with high transparency of the lungs, a large retrosternal air-filled space, and a flattened to concave diaphragm. The chest X-ray of the same subject (b) is shown 3 months after LVRS: the lung fields are less transparent, the air-filled retrosternal space decreased significantly, and the diaphragm exhibits an almost normal, convex shape.

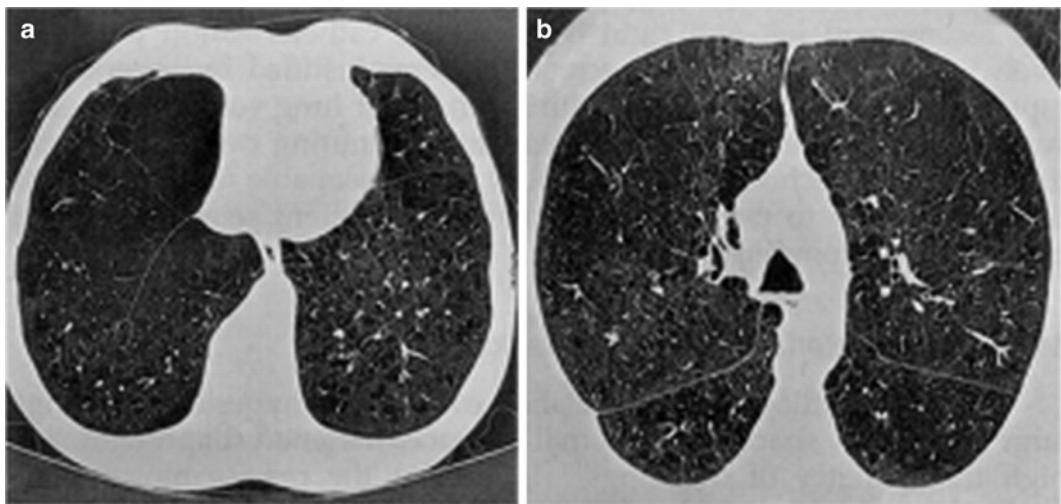
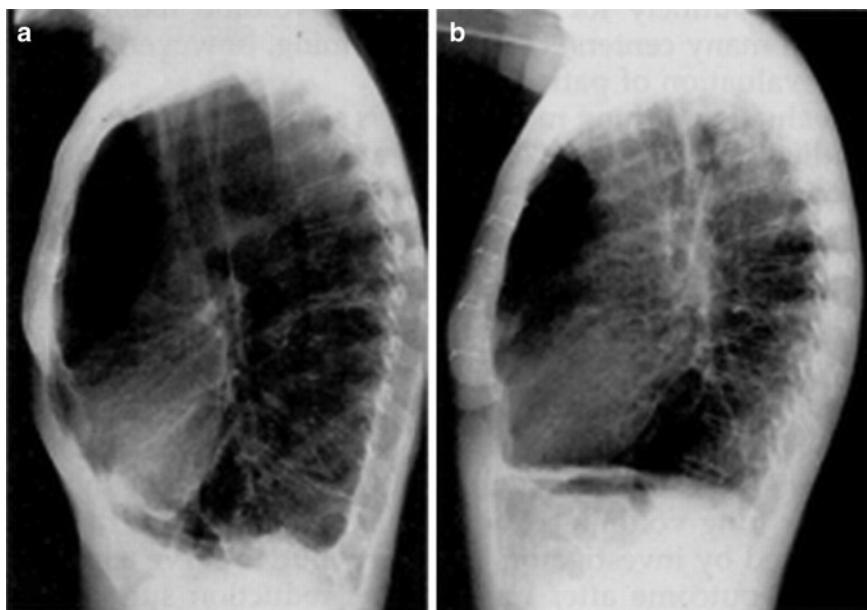


FIG. 36.2. (a) Depicts a high-resolution computed tomography (HR-CT) scan of a patient presenting with inhomogeneous distribution of emphysema. Parenchymal destruction is greater in the ventral portions of the lung; thus, the functional portions are easily distinguished from nonfunctional segments. (b) Depicts a HR-CT of a patient with homogeneous distribution of emphysema. It is much more difficult to determine which segments need to be resected.

be superior compared to lung perfusion scintigraphy for the evaluation of patients [26].

The evaluation of lung morphology is semi-quantitative and difficult to standardize. Only about 25% of patients present with inhomogeneous distribution of the disease. Therefore, the evaluation of preoperative functional criteria as predictors seems important.

Physiologic Evaluation

Currently, a preoperative $FEV_1 < 20\%$ of the predicted value in combination with homogenous morphology or a carbon

monoxide diffusion capacity $< 20\%$ of the predicted value is regarded as contraindication for surgery. These patients were found to have significantly increased mortality after LVRS compared with conventional medical treatment alone [27].

Pulmonary mechanics are severely impaired in patients suffering from emphysema, and LVRS leads to a significant improvement [28–33]. Several parameters characterizing pulmonary mechanics show specific changes after LVRS. Investigators tested these parameters as preoperative predictors for outcome after LVRS. FEV_1 is frequently chosen to represent outcome since it correlates well with mortality in emphysema patients. Furthermore, outcome is frequently characterized by

changes seen in pressure volume loops and by changes in dyspnea score since severe dyspnea leads to an impaired quality of life.

Ingenito et al. hypothesized that patients with markedly elevated inspiratory resistance are likely to have predominantly airway disease and are unlikely to show improvement of expiratory flow after LVRS thus, limiting the benefit of the procedure [34]. The investigators proved their hypothesis by demonstrating that preoperative inspiratory lung resistance negatively correlated with changes in FEV_1 (L) ($r=-0.63$; $p<0.001$). In contrast, patients with elevated expiratory lung resistance showed good improvement.

Preoperative PEEP_i, a correlate of dynamic pulmonary hyperinflation, and postoperative gain in normalized FEV_1 % predicted was found to be well correlated ($r=0.69$, $p<0.0002$) [35]. A cutoff point of preoperative PEEP_i of 5 cmH₂O had a positive predictive value of 86% and a negative predictive value of 92% in predicting a change in FEV_1 % of greater than 40% after LVRS [35]. Similar results were found for changes in dyspnea score.

Despite these and other promising methods to predict outcome following LVRS, most require time-consuming and sophisticated measuring techniques and are difficult to incorporate into standard clinical practice. As a result, none of the evaluated parameters has gained widespread acceptance to date.

Approach: Surgical vs. Bronchoscopic

Video-Assisted Thoracoscopic Surgery (VATS)

Surgery has been proven to be of benefit for selected patients with severe forms of emphysema in comparison to medical therapy alone and it has also been used as a bridging technique to lung transplantation [36]. LVRS has been reported to be cost-effective [4] and significantly improve pulmonary function, exercise tolerance, quality of life and even survival for a select patient population [37]. Patients with upper-lobe predominant emphysema and low exercise capacity demonstrated improved survival at 5 years, an increased exercise capacity throughout 3 years, and an improvement in overall symptoms through 5 years [38]. The results of the procedure are comparable whether performed through a median sternotomy or by video-assisted thoracoscopic surgery (VATS) [37]; however, the NETT indicated that the VATS approach provided earlier patient recovery compared with median sternotomy and it was more cost-effective [37]. LVRS has also been used in lung transplant recipients when the donor lungs have been deemed too large for the recipient's thoracic cavity.

The selection criteria for LVRS have been described in the previous section. Perhaps the most important selection factor for LVRS is the presence of a heterogenous pattern of emphysema and only about 20% of patients with severe emphysema satisfy this prerequisite. The goal for LVRS is to resect the

nonfunctional areas of the lung that constitute dead space and compress more functional lung segments, thus allowing the functional lung segments to expand and improve gas exchange. A bilateral staple procedure performed under general anesthesia and sequential single-lung ventilation is required.

Bronchoscopic Placement of Endobronchial Valves and Blockers

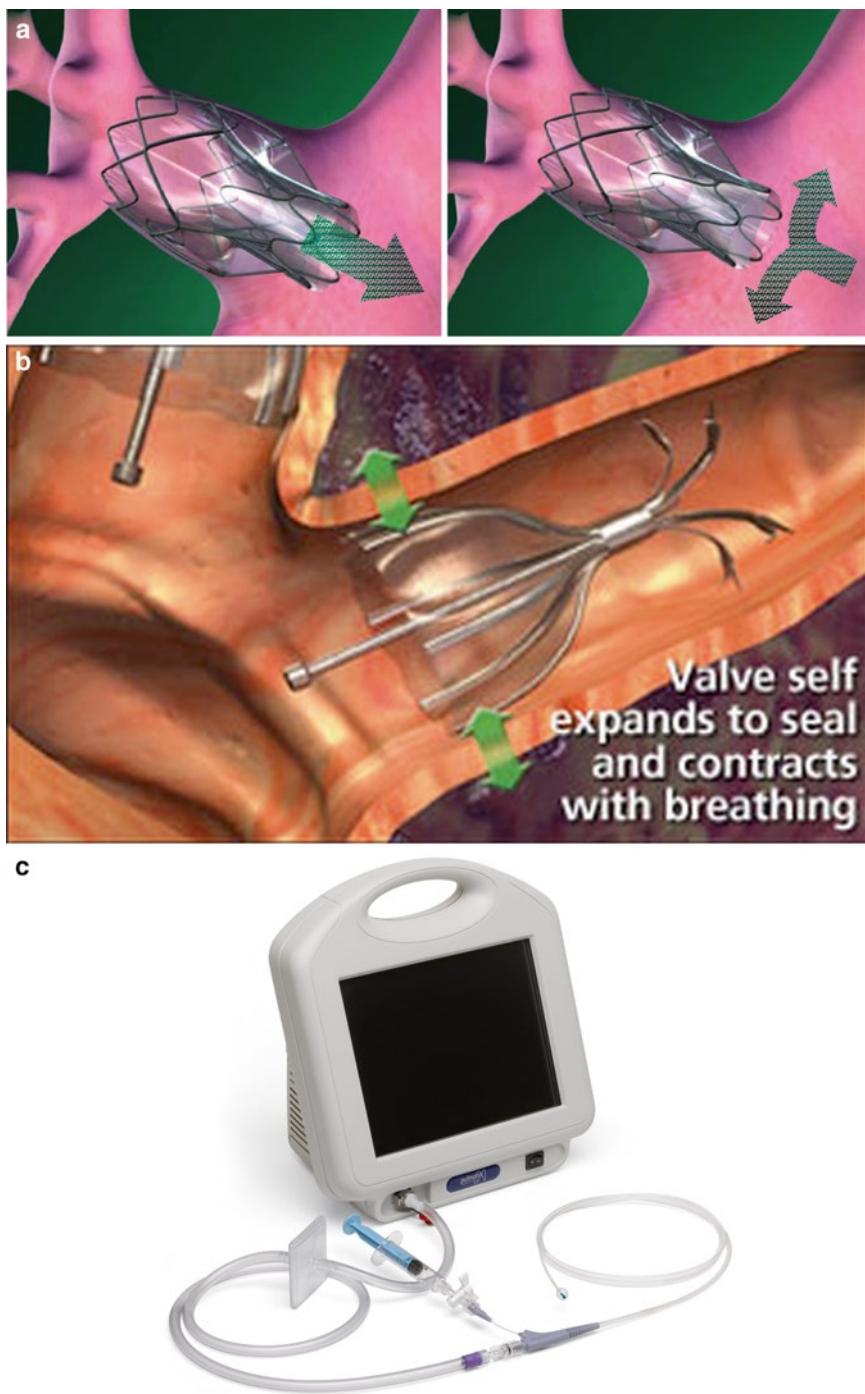
Although LVRS has been shown to be beneficial for patients with a heterogenous pattern of emphysema, this constitutes only about 20% of patients who are eligible candidates for this treatment. Procedures for bronchoscopic LVRS have thus been developed to treat patients with heterogenous and homogeneous patterns of emphysema. The rationale for this minimally invasive approach is that by endobronchially obstructing the emphysematous areas of the lung, collapse of these selected segments should occur, thereby reducing hyperinflation and alleviating symptoms without the need for surgery. Currently available bronchoscopic techniques include endobronchial blockers/valves, biologic glues, and airway bypass.

Figure 36.3 depicts blocker and valve devices currently for investigational use in the United States for LVRS in patients with heterogenous emphysema. These devices are placed in the patient's segmental bronchi to obstruct the flow of air into the selected segment while allowing air and mucus to escape via a one-way valve (Zephyr®EBV, PulmonX and IBV valves, Spiration, Inc.) or around the device (IBV valve, Spiration, Inc.). Both devices are compressed and are placed under direct vision using a fiberoptic bronchoscope and general anesthesia. An advantage of this technique, besides avoiding the risks of surgical LVRS, is that the devices may be repositioned or removed if necessary.

Preliminary outcome studies for these devices show promise and pivotal randomized trials are underway. Improvements in FEV_1 , residual volume, 6-min walk test, St. George Respiratory Questionnaire and Medical Research Council median dyspnea score have been demonstrated after insertion of the EBV valve and 43% of the patients were able to discontinue use of supplemental oxygen [39, 40]. Results for the IBV device are still pending.

Although there are significant improvements achieved with endobronchial blockers/valves, the results have not been as substantial as those obtained with surgical LVRS. Evaluation with ventilation/perfusion scans demonstrates that in some cases, the desired atelectasis to emulate surgical LVRS has occurred in a nonsustained manner. It is thought that collateral ventilation due to the presence of incomplete fissures might be implicated [41]. PulmonX has developed an adjunct detection device, the Chartis System (see Fig. 36.3c) that can directly assess collateral ventilation in the target lobe, a key criteria for identifying patients who will respond well to Zephyr® valve therapy. Chartis collateral flow screening must be performed under moderate sedation with the patient breathing normally in order to obtain an accurate assessment.

FIG. 36.3. (a) Depicts the Zephyr®EBV (registered trademark of PulmonX, Inc.). (b) Depicts the IBV (Spiration, Inc.). Both devices have been used to provide bronchoscopic LVRS for patients with heterogenous forms of emphysema. (c) Depicts the Chartis system (PulmonX) that is used to detect collateral flow and determine the suitability of patients for the Zephyr® EBV. A hollow balloon-tipped catheter is used to obstruct a lobar or segmental bronchus. Collateral flow to the obstructed region can be detected by measuring continued expired gas flow distal to the balloon (reprinted with permission from © 2010 PulmonX, Inc. All Rights Reserved).



Another alternative to combat less optimal results in bronchoscopic lung volume reduction for heterogenous emphysema was developed by Ingenito et al. He and his colleagues developed a transbronchoscopic technique to create and maintain volume loss using a washout solution and fibrin-based glue to collapse, seal and scar target regions of abnormal lung [42]. Initial results show that in short-term follow up there

was improved mean vital capacity, reduced mean residual volume, reduced mean residual volume/total lung capacity ratio, longer mean 6-min walk distance, and improved mean dyspnea score [43].

There is a device designed to reduce lung volume for patients with heterogenous or homologous emphysema and it is effective even when there are compromises in the fissures



FIG. 36.4. TheRePneu™ lung volume reduction device (PneumRx, Mountain View, CA) is designed to reduce lung volume for both heterogenous and homologous forms of emphysema. It is effective even when collateral ventilation due to compromises in the fissures between lung lobes exists. The preformed coil is delivered into a segmental or subsegmental bronchus in a straight configuration via a fiberoptic bronchoscope. After deployment, the device resumes its coil shape gathering and compressing emphysematous lung tissue.

between lung lobes. The RePneu™ LVRC (see Fig. 36.4) is constructed of Nitinol, that is preformed in a coil shape and that can be deployed into a target lobe via a bronchoscope and using either moderate sedation or general anesthesia. Multiple implants are used to obtain optimal results. This device is completely removable and preclinical studies have indicated that lung volume reduction of up to 50% has been achieved in human lungs.

Anesthetic Management

Preoperative Assessment

Pharmacologic Preparation

Most of the patients presenting for LVRS require long-term bronchodilator therapy (beta adrenergic agonists), steroid therapy (inhalation or systemic), and mucolytic therapy. Additionally, these patients frequently require antibiotics. Most centers recommend continuation of bronchodilator and mucolytic therapy before LVRS, including the day of surgery. The patient must be free from respiratory infections for at least 3 weeks prior to LVRS and require no antibiotic therapy preoperatively. In terms of steroid therapy, the goal is to gradually reduce the dose of systemic steroids prior to LVRS.

Many patients have received chronic theophylline therapy before LVRS and some patients experience toxic symptoms while theophylline blood levels are in the therapeutic range [44]. The main side-effects are nervousness, tremor, and tachycardia. Theophylline therapy should be discontinued before LVRS if the patient shows significant side-effects or if the serum levels are >20 ng/mL.

Pain Management

Thoracic Epidural Analgesia

By now it is a generally accepted concept that thoracic epidural analgesia (TEA) is mandatory for optimal postoperative pain management following LVRS. A thoracic epidural catheter is inserted at the T3-4 or T4-5 vertebral level in the awake patient immediately prior to surgery. The spread of anesthesia and analgesia should be assessed carefully before induction of general anesthesia in order to avoid inadequate pain management that may cause ventilatory depression during the immediate postoperative period. A local anesthetic such as bupivacaine or ropivacaine can be used for TEA preferably in combination with an opioid. Since emphysema patients tend to be volume depleted, it is important that they are adequately volume loaded (1–2 mL/kg) before fully activating the TEA so as to avoid severe hypotension. A potent vasopressor such as norepinephrine or phenylephrine should be available before activating the TEA. Ropivacaine is frequently preferred over bupivacaine as the local anesthetic since it causes less circulatory depression and helps to reduce the incidence of hypotension.

Most anesthesiologists providing care to patients for LVRS are convinced that TEA is crucial to reduce perioperative patient morbidity and mortality. Unfortunately, there are no controlled studies available to validate this theory. Some anesthesiologists might consider such a study unethical since patients would potentially be denied optimal pain management. In patients with normal lung function undergoing lung resection there is evidence that sufficient postoperative analgesia with TEA can reduce morbidity and mortality [45]; however, other authors emphasize that the influence of TEA on outcome after lung resection has not been proven [46]. Nevertheless, the use of TEA is the worldwide established means for intraoperative and postoperative analgesia for patients undergoing LVRS. In order to guarantee optimal analgesia, TEA should be maintained until all chest drains are removed.

Paravertebral Nerve Block

Paravertebral nerve blocks are multiple-level intercostal nerve blocks that have replaced the direct and multiple applications of local anesthetics to intercostal nerves, cryotherapy, and interpleural local anesthetics [47]. Paravertebral nerve blocks may be performed either by multiple injections or by inserting a catheter into the paravertebral space for use with a continuous infusion of local anesthetic [48, 49]. The levels of analgesia and restoration of pulmonary function seen with TEA can also be achieved with paravertebral nerve block when a multimodal analgesic regimen including the use of intravenous opioids and nonsteroidal anti-inflammatory agents (NSAIDS) are added. Outcome studies of the effect of paravertebral nerve blocks on morbidity and mortality rates following thoracic surgery, in particular LVRS,

have yet to be determined. It is widely accepted that the use of multimodal analgesia in conjunction with paravertebral nerve block is an excellent alternative to TEA. Paravertebral catheters may be inserted either percutaneously or under direct vision during thoracotomy. This technique is particularly useful for patients in whom placement of TEA is difficult or contraindicated.

Intraoperative Management

Monitors

Monitors for LVRS should include a six-lead ECG, pulse oximetry, invasive blood pressure monitoring, a temperature probe for continuous core temperature measurement, and a central venous catheter to assess central venous pressure. The routine use of a pulmonary artery catheter is controversial, however, continuous monitoring of pulmonary artery pressure (PAP) may be helpful since PAP can increase substantially during single lung ventilation thus, causing acute right ventricular failure. Transesophageal echocardiography may also be useful for intraoperative cardiac monitoring.

General Anesthesia

During endotracheal intubation with a double lumen tube, the intravenous analgesic requirement can be substantially reduced if the pharynx and larynx are carefully anesthetized with a topical anesthetic spray (e.g., 2% lidocaine) [50]. Following intubation, analgesia should be maintained with TEA. It is important to mention that intubation of a poorly anesthetized emphysema patient can precipitate life-threatening bronchospasm [51].

Only short-acting drugs should be used for sedation and neuromuscular blockade during general anesthesia for LVRS in order to facilitate tracheal extubation as early as possible after the procedure in order to avoid prolonged air leakage associated with prolonged positive pressure ventilation. Propofol is therefore a suitable choice for sedation. If the patient is susceptible to bronchospasm, a volatile inhalation anesthetic such as sevoflurane or isoflurane may be preferred over an intravenous agent. Neuromuscular blocking agents with short duration and absence of histamine liberation (e.g., vecuronium or cisatracurium) are frequently chosen.

Sufficient patient warming can be achieved using warming blankets, heating mats, and warm intravenous fluid infusions. Core body temperature and the peripheral temperature of the patient should be maintained within the normal range. A decrease in the body heat content of the patient will ultimately lead to shivering after extubation along with increased carbon dioxide production and oxygen consumption. It is frequently impossible for the end-stage emphysema patient to meet the increased ventilatory demands caused by shivering. Shivering is an undesirable complication that may lead to reintubation in the postoperative period.

Mechanical Ventilation

Optimal mechanical ventilation for LVRS must provide sufficient arterial oxygenation while strictly avoiding air trapping [18], which can potentiate the threat of pneumothorax. Air-trapping can be minimized by using moderate tidal volumes (≤ 9 mL/kg during ventilation of both lungs and ≤ 5 mL/kg during single lung ventilation), low respiratory frequencies (≤ 12 breaths/min during ventilation of both lungs and ≤ 16 breaths/min during single lung ventilation), and a prolonged expiratory time (I:E = 1:3 during double and single lung ventilation). If the preoperative HR-CT exhibits a substantial difference in the quality of lung tissue between the right and left lung, it may be more desirable to resect the less functional lung first.

It is important to limit airway pressure generated (≤ 35 cmH₂O) by the ventilator in order to avoid barotraumas resulting in a pneumothorax or tension pneumothorax. The anesthesiologist should pay constant attention to the inspired and expired volumes during mechanical ventilation. For this purpose it is necessary to monitor the configuration of the end-tidal CO₂ waves closely. In most patients undergoing LVRS, the anesthesiologist will have to accept elevated values of end-tidal and P_aCO₂ (arterial carbon dioxide tension) during single lung ventilation. This permissive hypercapnia is the price for the prevention of barotrauma during mechanical ventilation for LVRS. P_aCO₂ values will return to the normal range soon after the procedure when both lungs can be ventilated again.

Early Extubation

It is difficult to avoid air leakage entirely despite the use of new surgical techniques that use staplers buttressed with bovine pericardium. Air leakage can be exacerbated by positive pressure ventilation, whereas the negative intrapleural pressure generated during spontaneous breathing minimizes air leakage. Therefore, early extubation after LVRS is of prime importance. Several criteria must be satisfied before the patient can be extubated (Table 36.2). Should the patient fail to meet all of these criteria, it is reasonable to stabilize the patient in a quiet environment such as an intensive care unit or the post anesthesia care unit before extubation. Successful extubation will usually be possible within 1–2 h and is not harmful to the patient. This is preferable to premature

TABLE 36.2. Extubation criteria after LVRS.

1. Patient awake and cooperative
2. Patient breathing sufficiently, i.e., rapid shallow breathing index (respiratory frequency per min/tidal volume in L) is below 70
3. Sufficient arterial oxygenation: S_aO₂ ≥ 92 while patient is breathing spontaneously (F_iO₂ ≤ 0.35)
4. Adequate pain management achieved
5. Patient core temperature $>35.5^{\circ}\text{C}$
6. No shivering
7. Stable hemodynamic conditions

extubation in the operating room followed by prolonged episodes of arterial hypoxemia.

Postoperative Management

More than 50% of patients who undergo LVRS experience a complication during the postoperative period. They include: (1) oversedation; (2) accumulation of airway secretions; (3) pneumothorax; (4) bronchospasm; (5) pulmonary embolism; (6) pneumonia; (7) persistent air leaks; (8) arrhythmias; (9) myocardial infarction, and (10) pulmonary embolism. Reintubation and mechanical ventilation are associated with a high morbidity and mortality.

The majority of patients are extubated in the operating room and rarely require reintubation during the initial 48 h. However, significant hypercarbia and acidosis may be present for several hours owing to the residual effects of the anesthesia or incomplete analgesia. Unlike other patients undergoing pulmonary resection, the chest tubes in these patients are attached to water-seal drainage without suction. The loss of elastic recoil and the obstructive physiology of the remaining lung make it resistant to the usual loss of volume associated with a postoperative pneumothorax. The fragile nature of the lungs renders them more susceptible to the adverse effects of increased transpulmonary pressure and overdistention that would be caused by chest tube suction. This has a tendency to increase the magnitude and prolong the duration of air leaks in these patients. Postoperative management is directed to minimize these adverse side-effects: (1) judicious pulmonary toilet; (2) bronchodilator therapy; (3) effective perioperative analgesia with TEA or paravertebral/multimodal analgesia, and (4) avoidance of systemic corticosteroids.

Summary

LVRS is a viable option for a select group of emphysema patients and endobronchial valves and blockers that are undergoing clinical trials in the United States hold much promise as a treatment alternative for all emphysema patients. Regardless of the selection of treatment modality, the goals are the same: improvements in dyspnea, exercise tolerance, quality of life, and prolonged patient survival.

Patient selection is of crucial importance for a successful outcome after LVRS. The anesthesiologist must be actively involved in patient selection since he or she will be responsible for the patient's immediate perioperative management. Patient history and preoperative status as well as the results obtained from the evaluation of chest X-rays, HR-CT scans, and catheterization of the right heart should be carefully weighed during the patient selection process. The careful selection and preoperative preparation of patients is essential to minimize perioperative complications and obtain a successful outcome. Furthermore, it has to be emphasized that the role of the anesthesiologist is of crucial importance for the successful conduct of LVRS.

Clinical Case Discussion

Case: A 58-year-old female patient with end-stage emphysema is scheduled for bilateral LVRS using a video-assisted thoracoscopic approach (VATS). She has a past medical history that is significant for smoking (60 pack years; quit for the past 2 years), hypertension, and atrial fibrillation that is controlled with metoprolol. Her other medication includes an 81-mg aspirin that she takes once per day. She successfully completed a preoperative exercise program 8 weeks ago. The patient is very anxious and wishes to speak with the anesthesiologist who will provide her care prior to the date of surgery.

Questions

- What additional preoperative preparation is necessary from a pulmonary standpoint?
- How will you treat the patient's anxiety?
- What will you recommend for perioperative pain management?
- What are your specific concerns regarding postoperative management?

Preoperative Pulmonary Preparation:

- Successful completion of a preoperative exercise program including a 6-min walk on a flat surface, bicycle ergometer, and weight lifting (see Sections "Preoperative Medical Management of Emphysema Patients")
- Continue supplemental oxygen use, bronchodilators, mucolytics up to and including the day of surgery (see Section "Pharmacologic Preparation")
- Gradually reduce the dose of steroids prior to surgery if they are being administered
- If the patient is receiving theophylline therapy and exhibiting symptoms of toxicity (nervousness, tremor, tachycardia) or if serum levels exceed 20 ng/mL, discontinue the drug
- Ensure that the patient is free from infection and does not require antibiotics for at least a 3-week period prior to surgery

Treatment of Anxiety:

- Untreated anxiety may precipitate an episode of acute bronchospasm, an increase in dynamic pulmonary hyperinflation, and dyspnea (see Section "Psychological Preparation")
- An effective way to allay a patient's anxiety is for the anesthesiologist to establish a good relationship with the patient prior to the date of surgery by scheduling a meeting in the anesthesia preoperative evaluation clinic
- Anxiolytic therapy may be necessary during the preoperative and perioperative period

Perioperative Analgesia:

- The patient is at high risk for perioperative pulmonary complications if analgesia is insufficient or ineffective

- The risk of pulmonary complications may be improved with the use of thoracic epidural or paravertebral analgesia (see Sections “Thoracic Epidural Analgesia” and “Paravertebral Nerve Block”)
- TEA or paravertebral nerve block catheters should be maintained until the chest drains are removed and the patient is tolerating oral pain medications

Postoperative Management: (see Sections “Early Extubation” and “Postoperative Management”)

- Air leakage can be exacerbated by positive pressure ventilation. Therefore, the patient should be extubated as soon as it is safe to do so, preferably in the operating room. It is safe, however, to maintain mechanical ventilation for 1–2 h following surgery and this is preferable to premature extubation and the subsequent development of arterial hypoxemia
- Fifty percent of LVRS patients develop a postoperative complication
- Reintubation and mechanical ventilation in the postoperative period are associated with a high morbidity and mortality
- Postoperative complications can be minimized by implementing judicious pulmonary toilet, bronchodilator therapy, effective pain management with thoracic epidural or paravertebral analgesia, and avoidance of systemic corticosteroids

References

1. Prevalence and incidence of chronic obstructive pulmonary disease. 2010. <http://www.cureresearch.com/c/copd/prevalence.html>. Accessed 24 Jan 2010.
2. Brantigan OC, Mueller E, Kress MB. A surgical approach to pulmonary emphysema. *Am Rev Respir Dis.* 1959;80(1 Pt. 2): 194–206.
3. Cooper JD, Lefrak SS. Is volume reduction surgery appropriate in the treatment of emphysema? Yes. *Am J Respir Crit Care Med.* 1996;153:1201–4.
4. McKenna Jr RJ, Benditt JO, DeCamp M, et al. Safety and efficacy of median sternotomy versus video-assisted thoracic surgery for lung volume reduction surgery. *J Thorac Cardiovasc Surg.* 2004;127:1350–60.
5. National Emphysema Treatment Trial Group. Rationale and design of the national emphysema treatment trial (NETT): a prospective randomized trial of lung volume reduction surgery. *J Thorac Cardiovasc Surg.* 1999;118:518–28.
6. Carrell RW, Jeppsson JO, Laurell CB, et al. Structure and variation of the human alpha-1-antitrypsin. *Nature.* 1982;298:329–34.
7. Janus ED, Phillips NT, Carrell RW. Smoking, lung function and alpha-1-antitrypsin deficiency. *Lancet.* 1985;1:152–4.
8. Potter WA, Olafsson S, Hyatt RE. Ventilatory mechanics and expiratory flow limitation during exercise in patients with obstructive lung disease. *J Clin Invest.* 1971;50:910–9.
9. Stubbing DC, Pengelly LD, Morse JLC, et al. Pulmonary mechanics during exercise in subjects with chronic airflow obstruction. *J Appl Physiol.* 1980;49:511–5.
10. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis.* 1987;136:225–44.
11. Buist AS, Sexton GJ, Nagy JM, Ross BB. The effect of smoking cessation and modification on lung function. *Am Rev Respir Dis.* 1976;114:115–22.
12. Cooper JD, Trulock EP, Triantafillou AN, et al. Bilateral pneumectomy volume reduction for chronic obstructive pulmonary disease. *J Thorac Cardiovasc Surg.* 1995;109:106–19.
13. Hughes RL, Davison R. Limitations of exercise reconditioning in COPD. *Chest.* 1983;83:241–9.
14. Sahn SA. Corticosteroid therapy in chronic obstructive pulmonary disease. *Pract Cardiol.* 1985;11(8):150–6.
15. Tager I, Speizer FE. Role of infection in chronic bronchitis. *N Engl J Med.* 1975;292:563–71.
16. Anthonisen NR. Long-term oxygen therapy. *Ann Intern Med.* 1983;99:519–27.
17. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemia chronic obstructive lung disease: a clinical trial. *Ann Intern Med.* 1980;91:391–8.
18. Tuxen DV, Lane S. The effects of ventilatory pattern on hyperinflation, airway pressures, and circulation in mechanical ventilation of patients with severe air-flow obstruction. *Am Rev Respir Dis.* 1987;136:872–9.
19. Weinmann GG, Hyatt R. Evaluation and research in lung volume reduction surgery. *Am J Respir Crit Care Med.* 1996;154: 1913–8.
20. Daniel TM, Barry BK, Chan MD, et al. Lung volume reduction surgery: case selection, operative technique, and clinical results. *Ann Surg.* 1996;223(5):526–33.
21. Wisser W, Klepetko W, Senbaklavaci O, et al. Chronic hypercapnia should not exclude patients from lung volume reduction surgery. *Eur J Cardiothorac Surg.* 1998;14:107–12.
22. Thurnheer R, Muntwyler J, Stammberger U, et al. Coronary artery disease in patients undergoing lung volume reduction surgery for emphysema. *Chest.* 1997;112(1):122–8.
23. Hamacher J, Block KE, Stammberger U, et al. Two years' outcome of lung volume reduction surgery in different morphologic emphysema types. *Ann Thorac Surg.* 1999;68:1792–8.
24. Rogers RM, Coxson HO, Sciruba FC, et al. Preoperative severity of emphysema predictive of improvement after lung volume reduction surgery – use of CT morphometry. *Chest.* 2000;118:1240–7.
25. Salzman SH. Can CT measurement of emphysema severity aid patient selection for lung volume reduction surgery? *Chest.* 2000;118:1231–2.
26. Thurnheer R, Engel H, Weder W, et al. Role of lung perfusion scintigraphy in relation to chest computed tomography and pulmonary function in the evaluation of candidates for lung volume reduction surgery. *Am J Respir Crit Care Med.* 1999;159(1): 301–10.
27. National Emphysema Treatment Trial Research Group. Patients at high risk of death after lung-volume-reduction surgery. *N Engl J Med.* 2001;345(15):1075–83.
28. Dueck R, Cooper S, Kapelanski D, Colt H, Clauser J. A pilot study of expiratory flow limitation and lung volume reduction surgery. *Chest.* 1999;116:1762–71.
29. Gelb AF, Zamel N, McKenna RJ, Brenner M. Mechanism of short-term improvement in lung function after emphysema resection. *Am J Respir Crit Care Med.* 1996;154:945–51.

30. Marchand E, Gayan-Ramirez G, De Leyn P, Decramer M. Physiological basis of improvement after lung volume reduction surgery for severe emphysema: where are we? *Eur Respir J*. 1999;13(3):686–96.
31. Sciurba FC, Rogers RM, Keenan RJ, Slivka WA, Gorcsan J, Ferson PF, Holbert JM et al. Improvement in pulmonary function and elastic recoil after lung-reduction surgery for diffuse emphysema. *N Engl J Med*. 1996;334:1095–9.
32. Brown ML, Landreneau RJ. Improvement in pulmonary function and elastic recoil after lung-reduction surgery for diffuse emphysema. *N Engl J Med*. 1996;334:1095–9.
33. Tschernko EM, Wisser W, Hofer S, et al. Influence of lung volume reduction on ventilatory mechanics in patients suffering from severe COPD. *Anesth Analg*. 1996;83:996–1001.
34. Ingenito EP, Evans RB, Loring SH, et al. Relation between preoperative inspiratory lung resistance and the outcome of lung-volume-reduction surgery for emphysema. *N Engl J Med*. 1998;338:1181–5.
35. Tschernko EM, Kritzinger M, Gruber EM, et al. Lung volume reduction surgery: preoperative functional predictors for postoperative outcome. *Anesth Analg*. 1999;88:28–33.
36. Todic M, Lardinois D, Imfeld S, et al. Lung – volume reduction surgery as an alternative or bridging procedure to lung transplantation. *Ann Thorac Surg*. 2006;82:208–13.
37. The National Emphysema Treatment Trial Research Group. Effects of lung volume reduction surgery versus medical therapy: results from the National Emphysema Treatment Trial. *New Engl J Med*. 2003;324:2059–73.
38. Naunheim KS, Wood DE, Mohnsenifar Z, et al. Long-term follow-up of patients receiving lung-volume reduction surgery versus medical therapy for severe emphysema by the National Emphysema Treatment Trial Research Group. *Ann Thorac Surg*. 2006;82:431–3.
39. Toma TP, Hopkinson NS, Hillier J, et al. Bronchoscopic volume reduction with valve implants in patients with severe emphysema. *Lancet*. 2003;361:931–3.
40. Yim AP, Hwong TM, Lee TW, et al. Early results of endoscopic lung volume reduction for emphysema. *J Thorac Cardiovasc Surg*. 2004;127:1564–73.
41. Salamitri J, Kalfi V, Kelly M, et al. ¹³³Xenon ventilation scintigraphy applied to bronchoscopic lung volume reduction techniques for emphysema: relevance of interlobar collaterals. *Int Med J*. 2005;35:97–103.
42. Ingenito EP, Reilly JJ, Mentzer SH, et al. Bronchoscopic volume reduction: a safe and effective alternative to surgical therapy for emphysema. *Am J Respir Crit Care Med*. 2001;164:295–301.
43. Reilly J, Washko G, Pinto-Plata V, et al. Biological lung volume reduction: a new bronchoscopic therapy for advanced emphysema. *Chest*. 2007;131:1108–13.
44. Weinberg M, Hendeles L. Methylxanthines. In: Weiss EB, Segal MS, Stein M, editors. *Bronchial asthma. Mechanisms and therapeutics*. 2nd ed. Little, Brown and Company: Boston. 1985.
45. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86(3):598–612.
46. Warner DO. Preventing postoperative pulmonary complications. *Anesthesiology*. 2000;92:1467–72.
47. Keenan DJM, Cave K, Langdon L, et al. Comparative trial of rectal indomethacin and cryoanalgesia for control of early post-thoracotomy pain. *Br Med J*. 1983;287:1335.
48. Karmakar MJ. Thoracic paravertebral block. *Anesthesiology*. 2001;95:771–80.
49. Hill SE, Keller RA, Stafford-Smith M, et al. Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures. *Anesthesiology*. 2006;104:1047–53.
50. Loehning RW, Waltemath CL, Bergman NA. Lidocaine and increased respiratory resistance produced by ultrasonic aerosols. *Anesthesiology*. 1976;44:306–10.
51. Brandus V, Joffe S, Benoit CV, et al. Bronchial spasm during general anesthesia. *Can Anesth Soc J*. 1970;17:269–74.

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Key Points

- Preoperative assessment of the underlying diagnosis allows for optimal intraoperative ventilation settings.
- Preoxygenation and a smooth induction are essential to avoid pulmonary hypertensive crises and acute right ventricular failure.
- Transesophageal echocardiography is an invaluable tool in the diagnosis and management of intraoperative hemodynamic instability.
- A fluid restriction strategy is adopted to reduce the risk of low pressure pulmonary edema.
- Adequate postoperative analgesia is imperative to facilitate extubation, satisfactory sputum clearance, and early mobilization.

Introduction

Lung transplantation (LT) is the treatment of choice for certain patients with end-stage lung disease or pulmonary vascular disease [1]. The term “lung transplantation” encompasses a group of operations, comprised of lobar transplant, single-lung transplant (SLT), double-lung transplant, bilateral sequential lung transplant (BSLT), and heart–lung transplant (HLT). The first reported human LT was performed in 1963 at the University of Mississippi [2]. Over the following 20 years outcomes were poor, with few recipients surviving beyond the first postoperative month. With the introduction of cyclosporin and the development of surgical techniques in the 1980s, long-term survival became possible [3]. Over the next decade there was a sharp increase in the number of transplants performed worldwide, which plateaued in the late 1990s, before steadily

increasing again in more recent years (Fig. 37.1) [1]. Median survival for adult LT is approximately 5 years (Fig. 37.2). Initial postoperative mortality is similar between SLT and BSLT. After 1 year, recipients of SLT have lower survival rates [1, 4–6], which may reflect a difference in the underlying disease process and age of the recipients.

Donor Organ Management

The potential donor patient is often cared for in a nontransplant critical care unit [7]. After the diagnosis of brain stem death (BSD) [8–13], the pathophysiological sequelae [14–17] must be appropriately managed to effectuate organ preservation. This includes intravenous fluid administration and vasoactive therapy to achieve a mean arterial pressure (MAP) above 70 mmHg; heart rate 60–120 beats per minute; and a central venous pressure (CVP) or pulmonary capillary wedge pressure (PCWP) between 6 and 10 mmHg [18, 19]. Intravenous fluid restriction and judicious use of diuretics help to reduce fluid accumulation in the lungs [20]. The use of “hormonal” therapy, comprised of thyroxine, methylprednisolone and vasopressin, has been shown to increase the number of transplantable organs [21–24]. Ventilatory settings are altered to protect the potential donor lungs. This includes the use of small tidal volumes (6–8 mL/kg), in conjunction with pressure-controlled ventilation, with appropriate positive end-expiratory pressure (PEEP) and recruitment maneuvers [20, 24]. Bronchoscopic pulmonary toilet is used to clear retained secretions. Basic critical care therapies, such as normothermia, appropriate antimicrobial use, nutrition, correction of electrolyte disturbances, and treatment of diabetes insipidus are essential [16, 18].

FIG. 37.1. Number of lung transplants reported by year. (Adapted from Christie et al. [1].)

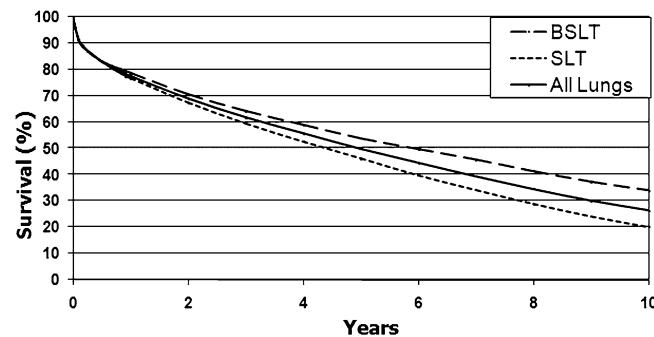
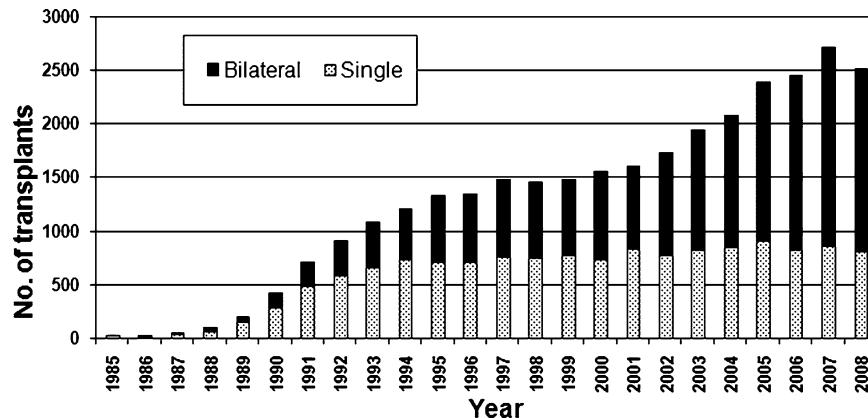


FIG. 37.2. Survival for adult lung transplantation 1996–2006. BSLT bilateral sequential lung transplant; SLT single lung transplant. (Adapted from Christie et al. [1].)

TABLE 37.1. Ideal donor lung criteria [29].

Age <55 years
Smoking history <20-pack years
ABO compatibility
Clear chest X-ray
Absence of chest trauma
Absence of pulmonary aspiration or purulent secretions on bronchoscopy
Absence of Gram stain negative bacteria and fungi
Arterial pO_2 >300 mmHg on FiO_2 1.0, PEEP 5 cmH ₂ O
FiO_2 fraction of inspired oxygen; PEEP positive end-expiratory pressure

Less than 20% of donors of other solid organs have lungs that are suitable for transplantation [20, 25]. This may be related to the etiology of BSD or secondary to the brain injury with the occurrence of pulmonary aspiration of gastric contents [26–28]. Due to the imbalance between the number of recipients awaiting transplantation and the availability of suitable donors, the “ideal” criteria [29] for donor lung acceptance (Table 37.1) have been extended by many centers. The survival of recipients from “marginal” donor organs appears to be similar to those from ideal donors [30–33], although there may be a higher incidence of primary graft dysfunction (PGD) [34, 35]. An alternative for extending the donor organ pool from BSD donors has been the development of ex-vivo lung reconditioning [36–38]. This method involves harvesting unacceptable



FIG. 37.3. Nonacceptable donor lungs undergoing ex-vivo reconditioning.

lungs, placing them on an ex-vivo circuit (Fig. 37.3) and optimizing their function prior to reassessment for transplantation. Early results from this technique are promising [39].

A shortage of organs from BSD donors has led to the use of patients in Maastricht category III [18] – the nonheart-beating donor (NHBD). Potential donors include patients in a critical care environment who are expected to die within 90 min of withdrawal of active treatment. Ethical considerations [40] mandate the use of two separate teams to be involved with the care of such a patient: one to decide to withdraw therapy and the second to perform organ procurement. Lung preservation interventions are withheld until cardiac death has been certified [41]. The lungs are unique in their ability to tolerate a warm ischemia time of at least 1 h [42, 43]. Outcomes of recipients from NHBD are comparable to those from BSD donors [44, 45].

During procurement, the donor receives systemic heparinization and the pulmonary artery is flushed with a cold preservation solution. The optimal pneumoplegia solution is still under debate [46–48]. Prior to preservation, a prostaglandin (typically PGE₁) is infused into the donor pulmonary circulation. This helps to inhibit the vasoconstrictive response to the cold pneumoplegia as well as being a potent inhibitor of platelet aggregation [49]. The bronchoscopic instillation of exogenous surfactant prior to procurement may improve post-operative graft function [50]. The donor lungs are ventilated with PEEP throughout the flush and are inflated to a pressure of 5–15 cmH₂O prior to dividing the airways [51, 52]. The harvested allograft is then stored at 4°C for transfer to the recipient centre.

Recipient Candidates

The international guidelines for the selection of lung transplant candidates were published in 1998 [53] and updated in 2006 [54]. Listing for transplantation should occur when life expectancy after transplantation exceeds life expectancy without the procedure. Donors and recipients are matched according to blood group and size. Due to the relative shortage of donor organs, it is essential to list only patients with realistic beneficial outcomes. Transplantation is indicated for patients with end-stage lung disease who are failing medical therapy, with the goal to provide a survival benefit [54]. The underlying disease processes responsible for LT referral include chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), idiopathic pulmonary fibrosis (IPF), pulmonary arterial hypertension (PAH), alpha-1 antitrypsin deficiency (AAT), and sarcoidosis (Fig. 37.4). The absolute contraindications are listed in Table 37.2. Relative contraindications include age over 65 years; severe obesity (body mass index greater than

30 kg/m²) [55]; severe osteoporosis; critical clinical condition, such as dependence upon mechanical ventilation or extracorporeal membrane oxygenation (ECMO); and colonization with resistant organisms [54].

Disease-specific indications for referral and listing for transplantation are summarized in Table 37.3. Patients suffering from emphysema can be assessed using the BODE index [56]. This includes scoring body mass index, airflow obstruction, degree of dyspnea, and exercise capacity on a scale from 0 to 10. A BODE index of 7–10 is associated with a lower survival than would be expected after transplantation. Lung volume reduction surgery may provide an alternative or a bridge to lung transplantation in such patients [57]. Cystic fibrosis patients may be colonized with resistant pathogens. Some studies suggest a higher mortality in CF patients infected with *Burkholderia cepacia* complex [58] and some centers refuse transplantation to this subpopulation [59]. Patients with IPF, also termed usual interstitial pneumonia (UIP), have the highest mortality on the transplant waiting list. For this reason,

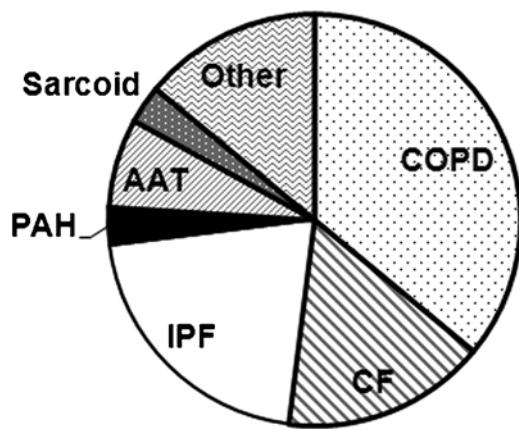


FIG. 37.4. Indications for lung transplantation. AAT alpha-1 antitrypsin deficiency; CF cystic fibrosis; COPD chronic obstructive pulmonary disease; IPF idiopathic pulmonary fibrosis; PAH pulmonary arterial hypertension. (Adapted from Christie et al. [1].)

TABLE 37.2. Absolute contraindications to lung transplantation [54].

Malignancy within previous 2 years (except cutaneous BCC and SCC) ^a
Advanced second major organ dysfunction (heart, liver or kidney) ^b
Chronic nonpulmonary infection (active hepatitis B and C; HIV)
Severe chest wall or spinal deformity
Untreatable psychiatric conditions
Substance addiction within previous 6 months
Noncompliance with medical therapy
Absence of reliable social support system

BCC basal cell carcinoma; HIV human immunodeficiency virus; SCC squamous cell carcinoma

^aFive-year disease-free survival is recommended

^bCoronary artery disease may be amenable to percutaneous or surgical intervention

TABLE 37.3. Disease-specific criteria for lung transplantation listing [54].

COPD/emphysema	FEV ₁ <20% predicted BODE index [56] of 7–10 Hospitalization with hypercapnia (pCO ₂ >50 mmHg) Pulmonary hypertension despite oxygen therapy
CF/bronchiectasis	Oxygen-dependent respiratory failure Hypercapnia Pulmonary hypertension
Pulmonary fibrosis	DLCO <39% predicted Decrease in SpO ₂ below 88% during 6-MWT Decrement >10% in FVC over 6 months Fibrosis score >2 on HRCT scan
Pulmonary hypertension	6-MWT <350 m Cardiac index <2 L/min/m ² Right atrial pressure >15 mmHg
Sarcoidosis	Hypoxemia at rest Pulmonary hypertension Right atrial pressure >15 mmHg

CF cystic fibrosis; COPD chronic obstructive pulmonary disease; DLCO diffusing capacity for carbon monoxide; FEV₁ forced expiratory volume in 1 s; FVC forced vital capacity; HRCT high-resolution computed tomography; SpO₂ pulse oximetry saturation; 6-MWT 6-min walk test

the lung allocation score (LAS) system [60] was developed to prioritize patients with the highest mortality risk before transplantation. The LAS system has been shown to decrease the wait-list time for patients with IPF [61]. Although most centers consider dependence on ECMO as a contraindication to LT, several reported case series have shown its use as a bridge to successful transplantation [62–64].

Anesthesia for Lung Transplantation

Preoperative Assessment

Due to the nature of lung transplantation, the anesthesiologist usually has limited time for preoperative assessment [65]. In some centers, the listed recipients are seen in an assessment clinic by an anesthesiologist to highlight important anesthetic considerations, such as potentially difficult intubations or chronic pain issues. Patients are generally debilitated, with poor cardiorespiratory reserve. Latent ischemic heart disease and right ventricular dysfunction are not uncommon, especially in the more elderly recipients [66–68], although the presence of noncritical coronary artery disease does not appear to influence postoperative outcomes [69]. Realistically, there is only time to employ a limited number of measures to optimize the recipient. These include chest physiotherapy to clear secretions, bronchodilator therapy, and drainage of pneumothoraces or large pleural effusions.

In addition to a routine thoracic patient assessment, preoperative evaluation should be focused on:

1. Underlying diagnosis: obstructive, suppurative or restrictive pulmonary defect. This will allow the anesthesiologist to select the most appropriate ventilatory settings for each patient [70].
2. Pulmonary artery pressure: this will dictate whether it will be possible to perform the procedure without the use of cardio-pulmonary bypass (CPB). Patients with severe pulmonary artery hypertension may benefit from preoperative or early intraoperative selective pulmonary vasodilator therapy [70].
3. Ventilation/perfusion (V/Q) scan: knowledge of the differential perfusion to each lung (in BSLT) will assist in deciding which lung will better tolerate pulmonary artery clamping and pneumonectomy.
4. Echocardiogram: in addition to providing an estimation of pulmonary artery systolic pressure [71], knowledge of right and left ventricular systolic function will influence the use of CPB.
5. Arterial blood gases (ABGs): preoperative measurement of ABGs provides a baseline pO_2/pCO_2 on which to base acceptable intraoperative limits.

Standard premedication usually involves immunosuppressant drugs, bronchodilator therapy, and supplemental oxygen. The routine use of anxiolysis is not advised and any sedative agents must be administered with great caution, as they may

exacerbate hypoxemia and hypercapnia, resulting in acute pulmonary hypertension and right ventricular failure.

Monitoring

Routine monitoring includes electrocardiography (ECG), pulse oximetry, invasive arterial and central venous pressure measurements, pulmonary artery catheterization (PAC), urinary catheter, temperature measurement, capnography and inhalational agent monitoring [72]. Minimally invasive cardiac output measurements, such as the esophageal Doppler monitor or pulse contour analysis devices, have been used in the nontransplant perioperative setting [73–76] and in nonpulmonary transplantation [77] with some degree of correlation to pulmonary artery thermodilution cardiac output measurements. Mixed venous oximetry has been used successfully in thoracic surgery, major cardiac surgery, and in nonpulmonary transplantation [78–80]. The use of continuous ABG [81, 82] monitoring would appear to provide an attractive monitor of rapid intraoperative alterations in pO_2 , pCO_2 and pH, but high costs have limited their widespread use [83]. Cerebral oximetry monitoring has been shown to improve outcomes in major cardiac surgery [84], but has not yet been proven in pulmonary transplantation. The use of bispectral index (BIS) to guide depth of anesthesia may reduce the incidence of awareness [85] and allow for more rapid recovery of patients [86]. The introduction of a closed-loop anesthesia delivery system using BIS [87, 88] provides better titration of drugs and accords the anesthesiologist more time to concentrate on managing intraoperative events.

Intraoperative hypothermia is known to provoke cardiac arrhythmias, coagulopathy [89] and result in increased postoperative infections [90]. Measurement of core body temperature is important in the early detection and prevention of inadvertent hypothermia [89].

Transesophageal Echocardiography

The use of transesophageal echocardiography (TEE) in pulmonary transplantation is a class IIb indication [91], suggesting it may be beneficial to patient outcome. TEE is more accurate in determining preload and filling status compared to the PAC [92]. It is invaluable in diagnosing the cause of any hemodynamic instability, including assessment of right ventricular (RV) function after clamping of the pulmonary artery [93–95], detection of gaseous emboli, and assessment of surgical anastomotic sites [96, 97]. Significant stenosis of pulmonary vein anastomoses, more commonly seen on the left (Fig. 37.5), leads to pulmonary venous congestion and may result in graft failure [98]. The presence of an atrial septal defect (ASD) or patent foramen ovale (PFO) can lead to a significant right to left shunt during periods of increased pulmonary vascular resistance (PVR), or when increased PEEP is employed [99]. Early detection by TEE can aid in diagnosing this cause of worsening arterial hypoxemia.

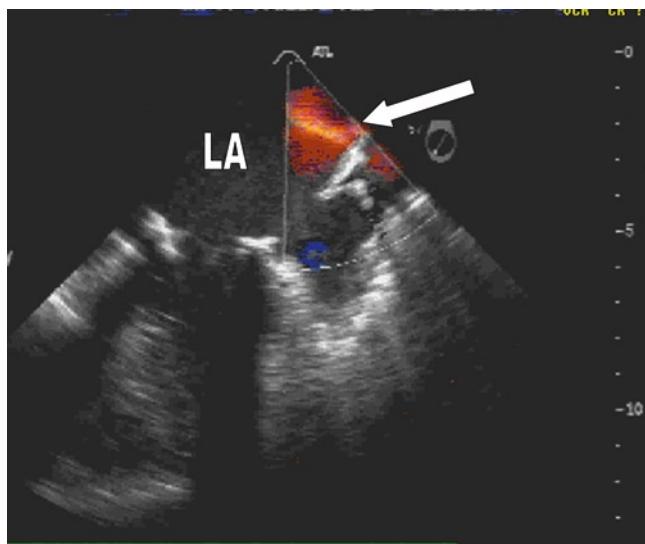


FIG. 37.5. Transesophageal echocardiography image of a stenotic left pulmonary vein anastomosis, highlighted by the turbulent color flow Doppler signal (arrow). LA left atrium.

Induction of Anesthesia

Preoxygenation of the patient prior to induction is recommended. The anesthesiologist must be aware that induction of anesthesia may precipitate cardiopulmonary collapse [100–102]. This is due to a combination of factors: systemic vasodilatation and negative inotropic effects of anesthetic drugs; an increase in intrathoracic pressure secondary to positive pressure ventilation, with a resultant reduced venous return [103]; hypercapnia due to hypoventilation, causing a rise in PVR and subsequent right ventricular failure [68].

In patients with obstructive lung pathologies it is important to allow sufficient time for the expiratory phase to occur and to avoid PEEP, in order to reduce the risk of hyperinflation [104]. Overenthusiastic manual ventilation immediately after induction of anesthesia can lead to severe gas-trapping in emphysematous lungs, resulting in reduced venous return and direct cardiac compression. Profound hypotension ensues and correct management is to disconnect the patient from the breathing circuit to allow sufficient time for expiration of trapped gases [105].

Patients with restrictive lung disease often require higher ventilatory pressures to deliver an adequate tidal volume and benefit from the application of increased levels of PEEP. Adoption of a ventilation strategy similar to that used in acute respiratory distress syndrome (reduced tidal volume, increased PEEP, and high respiratory rate) would seem more appropriate for this group of patients [106].

Recipients with suppurative pathologies may have mixed obstructive/restrictive pulmonary defects, so appropriate ventilation must be set according to each individual patient. Thorough bronchial lavage after intubation of the patient may reduce

intraoperative sputum plugging and assist in maintaining adequate ventilation throughout the procedure.

In patients with pulmonary vascular disease, smooth induction of anesthesia is critical to prevent hypertensive crises, myocardial depression, hypoxemia, and hypercapnia. Invasive central venous monitoring and PA catheters are generally inserted prior to induction. Acute management is directed at maintaining positive chronotropy and inotropy, optimization of preload and afterload, and reduction of intrathoracic pressures [70, 107]. Ketamine may be a more appropriate induction agent in severe cases, with vasoactive infusions commenced prior to induction. The use of inhaled pulmonary vasodilators [108] and preinduction ECMO [109] have been described. Emergency institution of CPB after induction may be required. The various disease-specific intraoperative complications are summarized in Table 37.4.

Following induction, intubation of the airway may be achieved with either a single-lumen or double-lumen tube (DLT). A single-lumen tube in combination with an endobronchial blocker [110] is an alternative to the use of a DLT. In BSLT, the blocker will need repositioning under bronchoscopic guidance to allow surgery on the opposite side. A left-sided DLT is preferred to a right-sided DLT, which may interfere with the right-sided bronchial anastomosis [70]. In patients with cystic fibrosis it is common to insert a single-lumen tube initially to facilitate bronchoscopic suctioning of thick secretions, prior to placing a DLT. Bronchoscopic washings are obtained from all patients after induction and sent for microbiological analysis, to assist in determining postoperative antimicrobial regimens.

Prophylactic antibiotic regimens are variable, but must provide adequate gram-positive and -negative cover. Patients with CF often require alternative antimicrobials, depending on their colonization and history of allergies.

TABLE 37.4. Disease-specific intraoperative anesthetic considerations.

Recipient pathology	Intraoperative complications
Emphysema (COPD, AAT)	Gas-trapping and auto-PEEP with positive pressure ventilation, leading to profound hypotension Older patients with concomitant coronary artery disease
Idiopathic pulmonary fibrosis	Higher ventilatory pressures required, causing reduced venous return Associated pathologies (e.g., scleroderma) Secondary pulmonary hypertension
Cystic fibrosis	Thick, tenacious secretions Small stature and multiple lung adhesions leading to difficult surgery and increased bleeding
Pulmonary hypertension	Difficult to maintain normocapnia Cardiovascular collapse at induction of anesthesia: CPB required
Bronchoalveolar carcinoma	Profuse watery secretions

AAT alpha-1 antitrypsin deficiency; COPD chronic obstructive pulmonary disease; CPB cardiopulmonary bypass; PEEP positive end-expiratory pressure

Maintenance of Anesthesia

Anesthesia may be maintained with either inhalational or intravenous agents [111–113]. Nitrous oxide may increase PVR [114] and should be avoided. SLT is usually performed through a standard thoracotomy, with the patient in the lateral position. BSLT may be performed either via a midline sternotomy, bilateral thoracotomies, or bilateral thoracotomy plus transverse sternotomy “Clamshell” incision (see Chap. 46, Fig. 46.4) [115, 116].

Initiation of one-lung ventilation (OLV) will initially precipitate an increased shunt and worsening hypoxemia, until surgical ligation of the pulmonary artery. During OLV, pressure-controlled ventilation may be preferable to volume-controlled ventilation, by reducing peak airway pressures [117, 118]. Patients unable to tolerate OLV will require the support of CPB [119] or ECMO [120].

Management of RV Dysfunction

Surgical clamping of the pulmonary artery (PA) during OLV will reduce shunt and improve oxygenation, but will lead to an acute increase in PA pressures. Right ventricular failure can occur and in high-risk patients it is prudent for the surgeon to apply temporary PA clamping for several minutes prior to definitive ligation [107]. Recipients with preexisting severe pulmonary hypertension rarely tolerate clamping of the PA and the elective use of CPB is employed [119, 121]. Prompt diagnosis of RV dysfunction by TEE [94] allows for suitable management and the possible avoidance of CPB. Acute elevation of PVR causes an increase in RV end-diastolic volume, leading to leftward shift of the interventricular septum (Fig. 37.6). Compliance of the LV is reduced, resulting in underfilling of the LV. Cardiac output falls and RV ischemia follows, with exacerbation of RV decompensation [107]. The use of inhaled nitric oxide (iNO) therapy reduces PVR, improves oxygenation, and can reverse RV failure [122–124]. Inhaled iloprost therapy is an alternative [125]. Positive inotropic agents, such

as epinephrine, will improve RV function. Phosphodiesterase inhibitors will provide inotropy and a reduction in PVR, but result in systemic vasodilatation, necessitating the addition of a vasoconstrictor, such as norepinephrine, to maintain coronary perfusion [126, 127]. The newer inotrope Levosimendan restores RV-PA coupling by decreasing PVR and increasing RV contractility [128] and may be beneficial in these patients.

Cardiopulmonary Bypass

There is institutional variation in preference for utilization of CPB. Elective use of CPB is indicated in recipients with severe pulmonary hypertension and in HLT. For BSLT with CPB, the heart remains warm and beating. After implantation of the first allograft, the heart is allowed to eject a little and the lung is gently ventilated. If performed without CPB, the lung receiving less perfusion (from the preoperative *V/Q* scan) should be replaced first. Unplanned use of CPB is reserved for patients with unmanageable hemodynamic instability, or those unable to tolerate OLV. Advantages of elective CPB are the avoidance of OLV and subsequent hypoxemia, hypercapnia and acidosis; improved surgical access; and limited duration of hemodynamic instability [129]. Disadvantages of CPB include increased crystalloid fluid loading resulting in pulmonary edema, heparinization with potential hemorrhage, systemic inflammatory response to CPB, coagulopathy, and reduced allograft function [130, 131]. Overall outcomes may be worse with the elective use of CPB [132–134]. Initiation of ECMO can provide an alternative to CPB if hypoxemia is the major problem [120, 135].

Fluid Management

Preload optimization is essential in managing intraoperative hemodynamics. However, the lung allograft is prone to low pressure pulmonary edema secondary to re-expansion injury,

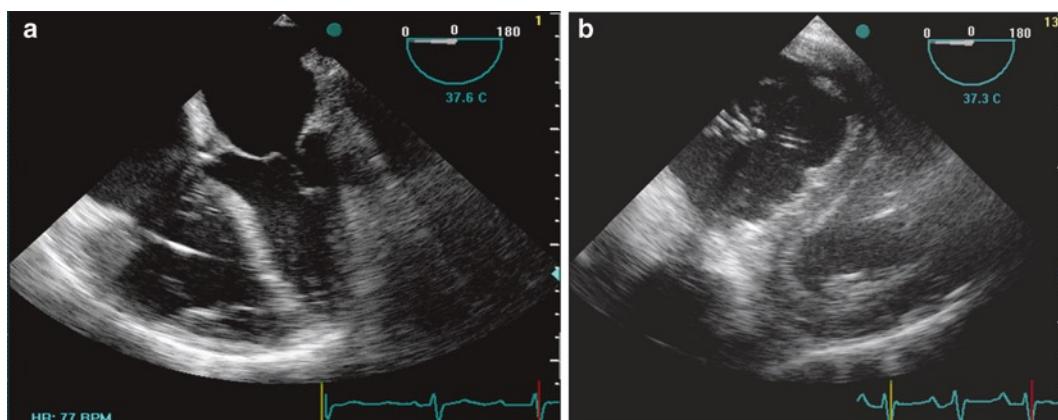


FIG. 37.6. Transesophageal echocardiography of right ventricular dilatation with classical flattening of the interventricular septum and shift toward the left ventricle, seen in the (a) mid-esophageal four-chamber and (b) transgastric short-axis views.

ischemia–reperfusion microvascular leak, and absence of lymphatic drainage [70, 106]. A restrictive fluid administration regimen, similar to that for pneumonectomy [136], is prudent, particularly when CPB is utilized. The use of the colloid Gelofusine (succinylated gelatin) has been linked to poorer postoperative allograft function and delayed extubation [137]. Red blood cells and blood products are transfused as appropriate. Although the liberal use of blood has been shown to be detrimental in the critically ill [138, 139], the associated immunomodulation may be beneficial to transplant recipients [140] and moderate exposure to allogeneic blood has been shown to be not detrimental in cardiac surgery with CPB [141].

The use of antifibrinolitics remains controversial. Recent evidence suggesting increased mortality with the use of aprotinin [142] excluded transplant operations, and patients undergoing LT, with or without CPB, appear to benefit from aprotinin administration [143, 144]. Tranexamic acid is an alternative antifibrinolytic agent.

Organ Reperfusion

Reperfusion of the allograft may result in hypotension, due to release of stored pneumoplegia and inflammatory mediators into the systemic circulation [65], and should occur gradually, over a period of approximately 10 min. Simultaneously, gentle ventilation is commenced with limited peak airway pressures, moderate PEEP (5–10 cm H₂O) and initially with a low fraction of inspired oxygen (FiO₂) [106, 145, 146]. In BSLT the residual native lung can be hand-ventilated with a high FiO₂ to maintain arterial oxygenation, whilst the new allograft is reperfusing with protective ventilation. After this initial period of reperfusion, the FiO₂ to the allograft is increased as necessary whilst ventilation to the native lung is stopped to enable surgical dissection. Ischemia–reperfusion (I–R) injury presents as hypoxemia despite increasing FiO₂, reduced lung compliance, pulmonary hypertension, and in severe cases with frank pulmonary edema. PGD [147] due to I–R is associated with an increased mortality [148]. The administration of iNO is effective in improving oxygenation in cases of I–R injury [149–151], but its routine use to prevent I–R injury is of less benefit [152, 153]. The perioperative use of aprotinin has been shown to have beneficial effects in terms of I–R injury and patient outcomes [154]. Severe hypoxemia due to reperfusion has been successfully treated with ECMO [155, 156].

Analgesia

In the postoperative period, insufficient pain control hinders spontaneous deep breathing, adequate coughing, and sputum clearance. Analgesic options comprise paracetamol; intravenous opiates, including patient-controlled analgesia; and regional techniques, including epidural and paravertebral analgesia. Opioid-sparing regimes are encouraged to reduce respiratory depression [106]. In some centers, the epidural is sited prior to surgery to facilitate earlier postoperative extubation.

Others prefer to insert the epidural at the end of the procedure or in the ICU immediately prior to extubation, after coagulopathy has been excluded. Paravertebral (epipleural) catheters can be placed by the surgeon at the end of an SLT as an alternative to epidural analgesia. There may be a role for low-dose intravenous ketamine to reduce postoperative opiate requirements [157]. Nonsteroidal anti-inflammatory agents are generally avoided due to the increased risk of renal dysfunction in patients receiving cyclosporin [158].

Postoperative Care

Early extubation in the operating room is feasible, particularly after SLT [159]. The advantages are avoidance of positive pressure ventilation, with associated barotrauma; improved oxygenation; reduced extravascular lung water; decreased PA pressures; lower requirement for vasoactive drug support; early mobilization and physiotherapy [160]. This is facilitated by short-acting anesthetic agents and epidural analgesia [159, 160]. For patients returning to the intensive care unit for postoperative ventilation, the DLT is changed for a single-lumen tube and a nasogastric tube is passed to facilitate early administration of enteral immunosuppression.

Ventilatory support involves a lung protective strategy [161] and potential differential lung ventilation in patients with SLT for emphysema [162]. Early tracheostomy is performed if prolonged ventilation is anticipated [163].

Early complications include PGD, which can be treated with iNO [149–151], ECMO [155, 156] and endobronchial instillation of surfactant [164]; hemorrhage (more commonly with CPB use), iatrogenic surgical anastomotic anomalies [165, 166]; infection [167–169]; cardiac arrhythmias [170]; renal failure [171]; venous thromboembolism [172]; and gastrointestinal pathologies [173]. Prevention of acute rejection is managed with a combination of steroids, calcineurin inhibitors, antiproliferatives, and mammalian target of rapamycin (mTOR) inhibitors. The routine use of induction therapy with monoclonal (Basiliximab) or polyclonal (antithymocyte globulin) antibodies is controversial, but may confer some survival benefit in BSLT [174].

Chronic allograft rejection is the major cause of late mortality [1] and typically presents as bronchiolitis obliterans. Infection and the development of malignancy are other causes of late mortality [175].

Clinical Case Discussion

Case: A 54-year-old male presents for elective laparoscopic cholecystectomy. He underwent right single-lung transplantation for emphysema (Fig. 37.7) 3 years previously. He has no other major co-morbidities. His preoperative pulmonary function tests show an FEV₁ of 1.6 L (69% predicted), FVC 2.5 L (78% predicted) and DLCO (84% predicted).

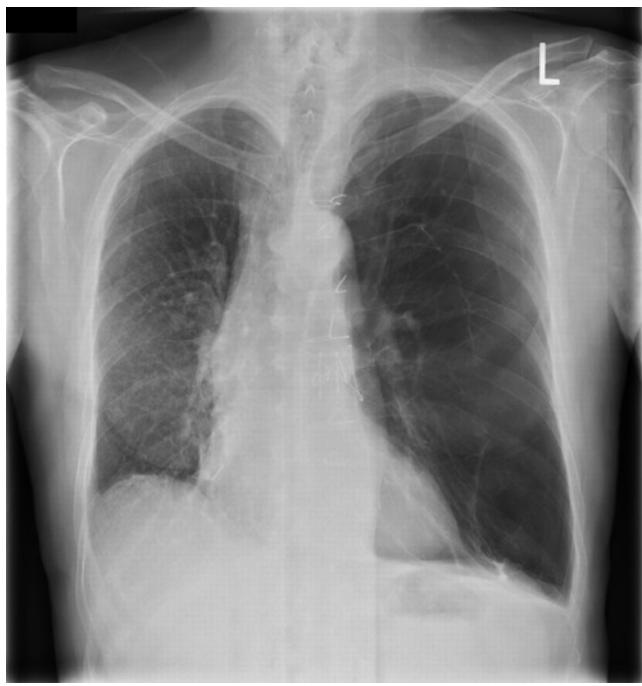


FIG. 37.7. Chest X-ray of a recipient of a right single-lung transplant.

Questions:

- What other transplant-related history is important?
- How would you ventilate the patient for this surgical procedure?
- What are the postoperative analgesic options?

Transplant-Related History

It is important to ascertain if the patient has had any recent episodes of allograft rejection, requiring pulsed high-dose steroid therapy and changes to his immunosuppression medication, or infective episodes, necessitating alterations to his antimicrobial regimen. Recent drug dose manipulations or drug alterations may have important interactions and effects on renal function.

Ventilation Strategy

As the patient's native lung is highly compliant and prone to gas-trapping, differential lung ventilation should be employed for this procedure. Positive pressure ventilation through a single-lumen endotracheal tube would preferentially force the anesthetic gas mixture into the native lung. Due to gas-trapping, hyperinflation would result, leading to direct cardiac compression, profound hypotension, and eventually cardiac arrest. A DLT should be positioned and normal ventilatory settings applied to the allograft lung. The native lung should receive only oxygen insufflation or low pressure ventilation with a prolonged expiratory phase.

Postoperative Analgesia

Multimodal analgesia should be employed, including paracetamol, opiates, and local anesthetic infiltration. If the laparoscopic surgery is converted to an open procedure, an epidural should be considered to avoid large doses of opiate. Nonsteroidal anti-inflammatory agents must be avoided due to their nephrotoxicity when used in combination with calcineurin inhibitors.

References

1. Christie JD, Edwards LB, Aurora P, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report-2009. *J Heart Lung Transplant*. 2009;28:1031–49.
2. Hardy JD, Webb WR, Dalton Jr ML. Lung homotransplantations in man: report of the initial case. *JAMA*. 1963;186:1065–74.
3. Toronto Lung Transplantation Group. Experience with single lung transplantation for pulmonary fibrosis. *JAMA*. 1988;259: 2258–62.
4. Cai J. Double- and single-lung transplantation: an analysis of twenty years of OPTN/UNOS registry data. *Clin Transpl*. 2007;1:1–8.
5. Hadjiliadis D, Angel LF. Controversies in lung transplantation: are two lungs better than one? *Semin Respir Crit Care Med*. 2006;27:561–6.
6. Chang AC, Chan KM, Lonigro RJ, et al. Surgical patient outcomes after the increased use of bilateral lung transplantation. *J Thorac Cardiovasc Surg*. 2007;133:532–40.
7. Liao WC, Hwang SL, Ko WJ, et al. Analysis of heart donation for cardiac transplantation at the National Taiwan University Hospital: fifteen-year cases review. *Transplant Proc*. 2004;36:2365–8.
8. Misis M, Raxach JG, Molto HP, et al. Bispectral index monitoring for early detection of brain death. *Transplant Proc*. 2008;40:1279–81.
9. Tatlisumak T, Forss N. Brain death confirmed with CT angiography. *Eur J Neurol*. 2007;14:42–3.
10. Monteiro LM, Bollen CW, van Huffelen AC, et al. Transcranial Doppler ultrasonography to brain death: a meta-analysis. *Intensive Care Med*. 2006;32:1937–44.
11. Young GB, Shemie SD, Doig CJ, et al. Brief review: the role of ancillary tests in the neurological determination of death. *Can J Anaesth*. 2006;53:620–7.
12. Morenski JD, Oro JJ, Tobias JD, et al. Determination of death by neurological criteria. *J Intensive Care Med*. 2003;18:211–21.
13. Wijdicks EF. The diagnosis of brain death. *New Engl J Med*. 2001;344:1215–21.
14. Palac RT, Summer G, Laird R, et al. Reversible myocardial dysfunction after traumatic brain injury. *Prog Transplant*. 2003; 13:42–6.
15. Dujardin DS, McCully RB, Wijdicks EF, et al. Myocardial dysfunction associated with brain death: clinical, echocardiographic, and pathologic features. *J Heart Lung Transplant*. 2001;20:350–7.
16. Smith M. Physiologic changes during brain stem death – lessons for management of the organ donor. *J Heart Lung Transplant*. 2004;23:S217–22.
17. Barklin A. Systemic inflammation in the brain-dead organ donor. *Acta Anaesthesiol Scand*. 2009;53:425–35.

18. Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: recommendations of the forum on medical management to optimize donor organ potential. *CMAJ*. 2006;174:S13–32.
19. Mascia L, Mastromauro I, Viberti S, et al. Management to optimize organ procurement in brain dead donors. *Minerva Anestesiol*. 2009;75:125–33.
20. Angel LF, Levine DJ, Restrepo MI, et al. Impact of a lung transplantation donor-management protocol on lung donation and recipient outcomes. *Am J Resp Crit Care Med*. 2006;174:710–6.
21. Follette DM, Rudich SM, Babcock WD. Improved oxygenation and increased lung donor recovery with high-dose steroid administration after brain death. *J Heart Lung Transplant*. 1998;17:423–9.
22. Venkateswaran RV, Patchell VB, Wilson IC, et al. Early donor management increases the retrieval rate of lungs for transplantation. *Ann Thorac Surg*. 2008;85:278–86.
23. Rosendale JD, Kauffman HM, McBride MA, et al. Aggressive pharmacologic donor management results in more transplanted organs. *Transplantation*. 2003;75:482–7.
24. Kutsogiannis DJ, Pagliarello G, Doig C, et al. Medical management to optimize donor organ potential: review of the literature. *Can J Anaesth*. 2006;53:820–30.
25. Winton TL. Lung transplantation: donor selection. *Semin Thorac Cardiovasc Surg*. 1992;4:79–82.
26. Weill D. Donor criteria in lung transplantation: an issue revisited. *Chest*. 2002;121:2029–31.
27. Gore SM, Taylor RM, Wallwork J. Availability of transplantable organs from brain stem dead donors in intensive care units. *BMJ*. 1991;302:149–53.
28. Orens JB, Boehler A, de Perrot M, et al. A review of lung transplant donor acceptability criteria. *J Heart Lung Transplant*. 2003;22:1183–200.
29. Van Raemdonck D, Neyrinck A, Verleden GM, et al. Lung donor selection and management. *Proc Am Thorac Soc*. 2009;15:28–38.
30. Bhorade SM, Vigneswaran W, McCabe MA, et al. Liberalization of donor criteria may extend the donor pool without adverse consequence in lung transplantation. *J Heart Lung Transplant*. 2000;19:1199–204.
31. Aigner C, Winkler G, Jaksch P, et al. Extended donor criteria for lung transplantation – a clinical reality. *Eur J Cardiothorac Surg*. 2005;27:757–61.
32. Fischer S, Gohrbandt B, Struckmeier P, et al. Lung transplantation with lungs from donors fifty years of age and older. *J Thorac Cardiovasc Surg*. 2005;129:919–25.
33. Whiting D, Banerji A, Ross D, et al. Liberalization of donor criteria in lung transplantation. *Am Surg*. 2003;69:909–12.
34. Kawut SM, Reyentovich A, Wilt JS, et al. Outcomes of extended donor lung recipients after lung transplantation. *Transplantation*. 2005;79:310–6.
35. Botha P, Trivedi D, Weir CJ. Extended donor criteria in lung transplantation: impact on organ allocation. *J Thorac Cardiovasc Surg*. 2006;131:1154–60.
36. Wierup P, Harraldsson A, Nilsson F, et al. Ex vivo evaluation of nonacceptable donor lungs. *Ann Thorac Surg*. 2006;81:460–6.
37. Steen S, Ingemansson R, Eriksson L, et al. First human transplantation of a nonacceptable donor lung after reconditioning ex vivo. *Ann Thorac Surg*. 2007;83:2191–4.
38. Cypel M, Yeung JC, Hirayama S, et al. Technique for prolonged normothermic ex vivo lung reperfusion. *J Heart Lung Transplant*. 2008;27:1319–25.
39. Ingemansson R, Eyjolfsson A, Mared L, et al. Clinical transplantation of initially rejected donor lungs after reconditioning ex vivo. *Ann Thorac Surg*. 2009;87:255–60.
40. Van Raemdonck D, Rega FR, Neyrinck A, et al. Non-heart-beating donors. *Semin Thorac Cardiovasc Surg*. 2004;16:309–21.
41. Oto T, Levvey B, McEgan R, et al. A practical approach to clinical lung transplantation from a Maastricht Category III donor with cardiac death. *J Heart Lung Transplant*. 2007;26:196–9.
42. Snell GI, Oto T, Levvey B, et al. Evaluation of techniques for lung transplantation following donation after cardiac death. *Ann Thorac Surg*. 2006;81:2014–9.
43. Egan TM. Non-heart-beating donors in thoracic transplantation. *J Heart Lung Transplant*. 2004;23:3–10.
44. Neyrinck AP, Van De Wauwer C, Geudens N, et al. Comparative study of donor lung injury in heart-beating versus non-heart-beating donors. *Eur J Cardiothorac Surg*. 2006;30:628–36.
45. De Vleeschauwer S, Van Raemdonck D, Vanaudenaerde B, et al. Early outcome after lung transplantation from non-heart-beating donors is comparable to heart-beating donors. *J Heart Lung Transplant*. 2009;28:380–7.
46. Aziz TM, Pillay TM, Corris PA, et al. Perfadex for clinical lung procurement: is it an advance? *Ann Thorac Surg*. 2003;75:990–5.
47. Oto T, Griffiths AP, Rosenfeldt F, et al. Early outcomes comparing Perfadex, Euro-Collins and Papworth solutions in lung transplantation. *Ann Thorac Surg*. 2006;82:1842–8.
48. Ganesh JS, Rogers CA, Banner NR, et al. Does the method of lung preservation influence outcome after transplantation? An analysis of 681 consecutive procedures. *J Thorac Cardiovasc Surg*. 2007;134:1313–21.
49. Chen CZ, Gallagher RC, Ardery P, et al. Retrograde flush and cold storage for twenty-two to twenty-five hours lung preservation with and without prostaglandin E1. *J Heart Lung Transplant*. 1997;16:658–66.
50. Struber M, Fischer S, Niedermeyer J, et al. Effects of exogenous surfactant instillation in clinical lung transplantation: a prospective, randomized trial. *J Thorac Cardiovasc Surg*. 2007;133:1620–5.
51. Haniuda M, Hasegawa S, Shiraishi T, et al. Effects of inflation volume during lung preservation on pulmonary capillary permeability. *J Thorac Cardiovasc Surg*. 1996;112:85–93.
52. Sundaresan S, Trachiotis GD, Aoe M, et al. Donor lung procurement: assessment and operative technique. *Ann Thorac Surg*. 1993;56:1409–13.
53. Maurer JR, Frost AE, Estenne M, et al. International guidelines for the selection of lung transplant candidates. *Transplantation*. 1998;66:951–6.
54. Oren JB, Estenne M, Arcasoy S, et al. International guidelines for the selection of lung transplant candidates: 2006 update – a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2006;25:745–55.
55. Kanasky Jr WF, Anton SD, Rodrigue JR, et al. Impact of body weight on long-term survival after lung transplantation. *Chest*. 2002;121:401–6.
56. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *New Engl J Med*. 2004;350:1005–12.
57. Tuttic M, Lardinois D, Imfeld S, et al. Lung-volume reduction surgery as an alternative or bridging procedure to lung transplantation. *Ann Thorac Surg*. 2006;82:208–13.

58. De Soya A, McDowell A, Archer L, et al. *Burkholderia cepacia* complex genomovars and pulmonary transplantation outcomes in patients with cystic fibrosis. *Lancet*. 2001;358:1780–1.
59. Levine SM. A survey of clinical practice of lung transplantation in North America. *Chest*. 2004;125:1224–38.
60. Egan TM, Murray S, Bustami RT, et al. Development of the lung allocation system in the United States. *Am J Transplant*. 2006;6:1212–27.
61. Iribarne A, Russo MJ, Davies RR, et al. Despite decreased wait-list times for lung transplantation, lung allocation scores continue to increase. *Chest*. 2009;135:923–8.
62. Jackson A, Cropper J, Pye R, et al. Use of extracorporeal membrane oxygenation as a bridge to primary lung transplant: 3 consecutive, successful cases and a review of the literature. *J Heart Lung Transplant*. 2008;27:348–52.
63. Santambrogio L, Nosotti M, Palleschi A, et al. Use of venovenous extracorporeal membrane oxygenation as a bridge to urgent lung transplantation in a case of acute respiratory failure. *Transplant Proc*. 2009;41:1345–6.
64. Fischer S, Simon AR, Welte T, et al. Bridge to lung transplantation with the novel pumpless interventional lung assist device NovaLung. *J Thorac Cardiovasc Surg*. 2006;131:719–23.
65. Myles PS. Aspects of anesthesia for lung transplantation. *Semin Cardiothorac Vasc Anesth*. 1998;2:140–54.
66. Thaik CM, Semigran MJ, Ginnis L, et al. Evaluation of ischemic heart disease in potential lung transplant recipients. *J Heart Lung Transplant*. 1995;14:257–66.
67. Leibowitz DW, Caputo AL, Shapiro GC, et al. Coronary angiography in smokers undergoing evaluation for lung transplantation: is routine use justified? *J Heart Lung Transplant*. 1994;13:701–3.
68. Vizza CD, Lynch JP, Ochoa LL, et al. Right and left ventricular dysfunction in patients with severe pulmonary disease. *Chest*. 1998;113:576–83.
69. Choong CK, Meyers BF, Guthrie TJ, et al. Does the presence of preoperative mild or moderate coronary artery disease affect the outcomes of lung transplantation? *Ann Thorac Surg*. 2006;82:1038–42.
70. Singh H, Bossard RF. Perioperative anaesthetic considerations for patients undergoing lung transplantation. *Can J Anaesth*. 1997;44:284–99.
71. Ben-Dor I, Kramer MR, Raccah A, et al. Echocardiography versus right-sided heart catheterization among lung transplantation candidates. *Ann Thorac Surg*. 2006;81:1056–60.
72. Quinlan JJ, Firestone S, Firestone LL. Anesthesia for heart, lung and heart-lung transplantation. In: Kaplan JA, Konstadt SN, Reich DL, editors. *Cardiac anesthesia*. 4th ed. Philadelphia, PA: WB Saunders; 1999. p. 991–1013.
73. Su NY, Huang CJ, Tsai P, et al. Cardiac output measurement during cardiac surgery: esophageal Doppler versus pulmonary artery catheter. *Acta Anaesthesiol Sin*. 2002;40:127–33.
74. Cannesson M, Attof Y, Rosamel P, et al. Comparison of FloTrac cardiac output monitoring system in patients undergoing coronary artery bypass grafting with pulmonary artery cardiac output measurements. *Eur J Anaesthesiol*. 2007;24:832–9.
75. Bein B, Worthmann F, Tonner PH, et al. Comparison of esophageal Doppler, pulse contour analysis, and real-time pulmonary artery thermodilution for the continuous measurement of cardiac output. *J Cardiothorac Vasc Anesth*. 2004;18:185–9.
76. Funk DJ, Moretti EW, Gan TJ. Minimally invasive cardiac output monitoring in the perioperative setting. *Anesth Analg*. 2009;108:887–97.
77. Perilli V, Avolio AW, Sacco T, et al. Use of an esophageal echo-Doppler device during liver transplantation: preliminary report. *Transplant Proc*. 2009;41:198–200.
78. Thys DM, Cohen E, Eisenkraft JB. Mixed venous oxygen saturation during thoracic anesthesia. *Anesthesiology*. 1988;69:1005–9.
79. Vederinne C, Bastien O, De Varax R, et al. Predictive factors for usefulness of fiberoptic pulmonary artery catheter for continuous oxygen saturation in mixed venous blood monitoring in cardiac surgery. *Anesth Analg*. 1997;85:2–10.
80. Jenstrup M, Ejlersen E, Rasmussen LS, et al. Mixed venous oxygen saturation and thoracic electrical impedance for fluid volume management during liver transplantation. *Transplant Proc*. 1994;26:1793.
81. Venkatesh B, Clutton Brock TH, Hendry SP. A multiparameter sensor for continuous intra-arterial blood gas monitoring: a prospective evaluation. *Crit Care Med*. 1994;22:588–94.
82. Venkatesh B, Clutton Brock TH, Hendry SP. Evaluation of the Paratrend 7 intravascular blood gas monitor during cardiac surgery: comparison with the C4000 in-line blood gas monitor during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*. 1995;9:412–9.
83. Venkatesh B. Continuous intra-arterial blood gas monitoring. *Crit Care Resusc*. 1999;1:140–50.
84. Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51–8.
85. Myles PS, Leslie K, McNeil J, et al. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *Lancet*. 2004;363:1757–63.
86. Puri GD, Murthy SS. Bispectral index monitoring in patients undergoing cardiac surgery under cardiopulmonary bypass. *Eur J Anaesthesiol*. 2003;20:451–6.
87. Liu N, Chazot T, Genty A, et al. Titration of propofol for anesthetic induction and maintenance guided by the bispectral index: closed-loop versus manual control: a prospective, randomized, multicenter study. *Anesthesiology*. 2006;104:686–95.
88. De Smet T, Struys MM, Neckebroek MM, et al. The accuracy and clinical feasibility of a new bayesian-based closed-loop control system for propofol administration using the bispectral index as a controlled variable. *Anesth Analg*. 2008;107:1200–10.
89. NICE clinical guideline 65: inadvertent perioperative hypothermia. <http://www.nice.org.uk/CG065>. Accessed 30 November 2009.
90. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med*. 1996;334:1209–15.
91. Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *Circulation*. 2003;108:1146–62.
92. Della Rocca G, Brondani A, Costa MG. Intraoperative hemodynamic monitoring during organ transplantation: what is new? *Curr Opin Organ Transplant*. 2009;14:291–6.
93. Haddad F, Couture P, Tousignant C, et al. The right ventricle in cardiac surgery, a perioperative perspective: anatomy, physiology, and assessment. *Anesth Analg*. 2009;108:407–21.

94. Pedoto A, Amar D. Right heart function in thoracic surgery: role of echocardiography. *Curr Opin Anaesthesiol*. 2009;22:44–9.
95. Katz WE, Gasior TA, Quinlan JJ, et al. Immediate effects of lung transplantation on right ventricular morphology and function in patients with variable degrees of pulmonary hypertension. *J Am Coll Cardiol*. 1996;27:384–91.
96. Michel-Cherqui M, Brusset A, Liu N, et al. Intraoperative transesophageal echocardiographic assessment of vascular anastomoses in lung transplantation: a report on 18 cases. *Chest*. 1997;111:1229–35.
97. Leibowitz DW, Smith CR, Michler RE, et al. Incidence of pulmonary vein complications after lung transplantation: a prospective transesophageal echocardiographic study. *J Am Coll Cardiol*. 1994;24:671–5.
98. Huang YC, Cheng YJ, Lin YH, et al. Graft failure caused by pulmonary venous obstruction diagnosed by intraoperative transesophageal echocardiography during lung transplantation. *Anesth Analg*. 2000;91:558–60.
99. Sukernik MR, Mets B, Bennett-Guerrero E. Patent foramen ovale and its significance in the perioperative period. *Anesth Analg*. 2001;93:1137–46.
100. Myles PS, Weeks AM, Buckland MR, et al. Anesthesia for bilateral sequential lung transplantation: experience of 64 cases. *J Cardiothorac Vasc Anesth*. 1997;11:177–83.
101. Hohn L, Schweizer A, Morel DR, et al. Circulatory failure after anesthesia induction in a patient with severe primary pulmonary hypertension. *Anesthesiology*. 1999;91:1943–5.
102. Myles PS, Weeks AM. Alpha 1-antitrypsin deficiency: circulatory arrest following induction of anaesthesia. *Anaesth Intensive Care*. 1992;20:358–62.
103. Manthous CA. Avoiding circulatory complications during endotracheal intubation and initiation of positive pressure ventilation. *J Emerg Med*. 2009;38(5):622–31.
104. Quinlan JJ, Buffington CW. Deliberate hypoventilation in a patient with air trapping during lung transplantation. *Anesthesiology*. 1993;78:1177–81.
105. Myles PS, Ryder IG, Weeks AM, et al. Diagnosis and management of dynamic hyperinflation during lung transplantation. *J Cardiothorac Vasc Anesth*. 1997;11:100–4.
106. Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, editors. *Thoracic anaesthesia*. 3rd ed. Philadelphia, PA: Churchill Livingstone. 2003;295–314.
107. Feltracco P, Serra E, Barbieri F, et al. Anesthetic considerations in lung transplantation for severe pulmonary hypertension. *Transplant Proc*. 2007;39:1976–80.
108. Snell GI, Salamonsen RF, Bergin P, et al. Inhaled nitric oxide as a bridge to heart-lung transplantation in a patient with end-stage pulmonary hypertension. *Am J Resp Crit Care Med*. 1995;151:1263–6.
109. de Boer WJ, Waterbolk TW, Brugemann J, et al. Extracorporeal membrane oxygenation before induction of anesthesia in critically ill thoracic transplant patients. *Ann Thorac Surg*. 2001;72:1407–8.
110. Scheller MS, Kriett JM, Smith CM, et al. Airway management during anesthesia for double-lung transplantation using a single-lumen endotracheal tube with an enclosed bronchial blocker. *J Cardiovasc Thorac Anesth*. 1992;6:204–7.
111. Abe K, Shimizu T, Takashina M, et al. The effects of propofol, isoflurane and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. *Anesth Analg*. 1998;87:1164–9.
112. Beck DH, Doepfmer UR, Sinemus C, et al. Effects of sevoflurane and propofol on pulmonary shunt fraction during one-lung ventilation for thoracic surgery. *Br J Anaesth*. 2001;86:38–43.
113. Pruszkowski O, Dalibon N, Moutafis M, et al. Effects of propofol vs sevoflurane on arterial oxygenation during one-lung ventilation. *Br J Anaesth*. 2007;98:539–44.
114. Schulte-Sasse U, Hess W, Tarnow J. Pulmonary vascular responses to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology*. 1982;57:9–13.
115. Macchiarini P, Ladurie F, Cerrina J, et al. Clamshell or sternotomy for double-lung or heart-lung transplantation? *Eur J Cardiothorac Surg*. 1999;15:333–9.
116. Taghavi S, Birsan T, Pereszlenyi A, et al. Bilateral lung transplantation via two sequential anterolateral thoracotomies. *Eur J Cardiothorac Surg*. 1999;15:658–62.
117. Tugrul M, Camci E, Karadeniz H, et al. Comparison of volume controlled with pressure controlled ventilation during one-lung anaesthesia. *Br J Anaesth*. 1997;79:306–10.
118. Unzueta MC, Casas JI, Moral MV. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation for thoracic surgery. *Anesth Analg*. 2007;104:1029–33.
119. Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg*. 1994;57:1248–51.
120. Bittner HB, Binner C, Lehmann S, et al. Replacing cardiopulmonary bypass with extracorporeal membrane oxygenation in lung transplantation operations. *Eur J Cardiothorac Surg*. 2007;31:462–7.
121. de Hoyos A, Demajo W, Snell G, et al. Preoperative prediction for the use of cardiopulmonary bypass in lung transplantation. *J Thorac Cardiovasc Surg*. 1993;106:787–95.
122. Rocca GD, Passariello M, Coccia C, et al. Inhaled nitric oxide administration during one-lung ventilation in patients undergoing thoracic surgery. *J Cardiovasc Thorac Anesth*. 2001;15:218–23.
123. Fierobe L, Brunet F, Dhainaut JF, et al. Effect of inhaled nitric oxide on right ventricular function in adult respiratory distress syndrome. *Am J Resp Crit Care Med*. 1995;15:1414–9.
124. Krasuski RA, Warner JJ, Wang A, et al. Inhaled nitric oxide selectively dilates pulmonary vasculature in adult patients with pulmonary hypertension, irrespective of etiology. *J Am Coll Cardiol*. 2000;36:2204–11.
125. Winterhalter M, Simon A, Fischer S, et al. Comparison of inhaled iloprost and nitric oxide in patients with pulmonary hypertension during weaning from cardiopulmonary bypass in cardiac surgery: a prospective randomized trial. *J Cardiothorac Vasc Anesth*. 2008;22:406–13.
126. Forrest P. Anaesthesia and right ventricular failure. *Anaesth Intensive Care*. 2009;37:370–85.
127. Martin C, Perrin G, Saux P, et al. Effects of norepinephrine on right ventricular function in septic shock patients. *Intensive Care Med*. 1994;20:444–7.
128. Kerbaul F, Gariboldi V, Giorgi R, et al. Effects of levosimendan on acute pulmonary embolism-induced right ventricular failure. *Crit Care Med*. 2007;35:1948–54.
129. Marcin N, Royston D, Yacoub M. Pro: lung transplantation should be routinely performed with cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*. 2000;14:739–45.
130. Gammie JS, Cheul Lee J, Pham SM, et al. Cardiopulmonary bypass is associated with early allograft dysfunction but not death after double-lung transplantation. *J Thorac Cardiovasc Surg*. 1998;115:990–7.

131. McRae K. Con: lung transplantation should not be routinely performed with cardiopulmonary bypass. *J Cardiothorac Vasc Anesth.* 2000;14:746–50.
132. Aeba R, Griffith BP, Kormos RL, et al. Effect of cardiopulmonary bypass on early graft dysfunction in clinical lung transplantation. *Ann Thorac Surg.* 1994;57:715–22.
133. Dalibon N, Geffroy A, Moutafis M, et al. Use of cardiopulmonary bypass for lung transplantation: a 10-year experience. *J Cardiothorac Vasc Anesth.* 2006;20:668–72.
134. Ferrer J, Rodriguez E, Roman A, et al. Factors related to postoperative mortality in lung transplantation for emphysema. *Transplant Proc.* 2007;39:3317–22.
135. Ko WJ, Chen YS, Lee YC. Replacing cardiopulmonary bypass with extracorporeal membrane oxygenation in lung transplant operations. *Artif Organs.* 2001;25:607–12.
136. Slinger PD. Perioperative fluid management for thoracic surgery: the puzzle of post-pneumonectomy pulmonary edema. *J Cardiothorac Vasc Anesth.* 1995;9:442–51.
137. McIlroy DR, Pilcher DV, Snell GI. Does anaesthetic management affect early outcomes after lung transplant? An exploratory analysis. *Br J Anaesth.* 2009;102:506–14.
138. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med.* 1999;340:409–17.
139. Vincent JL, Baron JF, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. *JAMA.* 2002;25:1499–507.
140. Cicciarelli J. UNOS registry data: effect of transfusions. *Clin Transpl.* 1990;407–16.
141. Weightman WM, Gibbs NM, Shemirant MR, et al. Moderate exposure to allogeneic blood products is not associated with reduced long-term survival after surgery for coronary artery disease. *Anesthesiology.* 2009;111:327–33.
142. Fergusson DA, Hebert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med.* 2008;358:2319–31.
143. Kesten S, de Hoyas A, Chaparro C, et al. Aprotinin reduces blood loss in lung transplant recipients. *Ann Thorac Surg.* 1995;59:877–9.
144. Balsara KR, Morozowich ST, Lin SS, et al. Aprotinin's effect on blood product transfusion in off-pump bilateral lung transplantation. *Interact Cardiovasc Thorac Surg.* 2009;8:45–8.
145. McRae K. Pulmonary transplantation. *Curr Opin Anaesthesiol.* 2000;13:53–9.
146. de Perrot M, Imai Y, Volgyesi GA, et al. Effect of ventilator-induced lung injury on the development of reperfusion injury in a rat lung transplant model. *J Thorac Cardiovasc Surg.* 2002;124:1137–44.
147. Christie JD, Carby M, Bag R, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part II: definition. A consensus statement of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant.* 2005;24:1454–9.
148. Cottini SR, Lerch N, de Perrot M, et al. Risk factors for reperfusion injury after lung transplantation. *Intensive Care Med.* 2006;32:557–63.
149. Macdonald P, Mundy J, Rogers P, et al. Successful treatment of life-threatening acute reperfusion injury after lung transplantation with inhaled nitric oxide. *J Thorac Cardiovasc Surg.* 1995;110:861–3.
150. Della Rocca G, Pierconti F, Costa MG, et al. Severe reperfusion lung injury after double lung transplantation. *Crit Care.* 2002;6:240–4.
151. Kemming GI, Merkel MJ, Schallerer A, et al. Inhaled nitric oxide for the treatment of early allograft failure after lung transplantation. *Munich Lung Transplant Group. Intensive Care Med.* 1998;24:1173–80.
152. Meade MO, Granton JT, Matte-Martyn A, et al. A randomized trial of inhaled nitric oxide to prevent ischemia-reperfusion injury after lung transplantation. *Am J Resp Crit Care Med.* 2003;167:1483–9.
153. Botha P, Jeyakanthan M, Rao JN, et al. Inhaled nitric oxide for modulation of ischemia-reperfusion injury in lung transplantation. *J Heart Lung Transplant.* 2007;26:1199–205.
154. Bittner HB, Richter M, Kuntze T, et al. Aprotinin decreases reperfusion injury and allograft dysfunction in clinical lung transplantation. *Eur J Cardiothorac Surg.* 2006;29:210–5.
155. Hsu HH, Ko WJ, Chen JS, et al. Extracorporeal membrane oxygenation in pulmonary crisis and primary graft dysfunction. *J Heart Lung Transplant.* 2008;27:233–7.
156. Khan NU, Al-Aloul M, Shah R, et al. Early experience with the Levitronix Centrimag device for extra-corporeal membrane oxygenation following lung transplantation. *Eur J Cardiothorac Surg.* 2008;34:1262–4.
157. Bell R, Dahl JB, Moore RA, et al. Perioperative ketamine for acute postoperative pain. *Cochrane Database Syst Rev.* 2006;25:CD004603.
158. Altman RD, Perez GO, Sfakianakis GN. Interaction of cyclosporine A and nonsteroidal anti-inflammatory drugs on renal function in patients with rheumatoid arthritis. *Am J Med.* 1992;93:396–402.
159. Hansen LN, Ravn JB, Yndgaard S. Early extubation after single-lung transplantation: analysis of the first 106 cases. *J Cardiothorac Vasc Anesth.* 2003;17:36–9.
160. Rocca GD, Coccia C, Costa GM, et al. Is very early extubation after lung transplantation feasible? *J Cardiothorac Vasc Anesth.* 2003;17:29–35.
161. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med.* 2000;342:1301–8.
162. Mitchell JB, Shaw AD, Donald S, et al. Differential lung ventilation after single-lung transplantation for emphysema. *J Cardiothorac Vasc Anesth.* 2002;16:459–62.
163. Waller EA, Aduen JF, Kramer DJ, et al. Safety of percutaneous dilatational tracheostomy with direct bronchoscopic guidance for solid organ allograft recipients. *Mayo Clin Proc.* 2007;82(12):1502–8.
164. Kermeen FD, McNeil KD, Fraser JF, et al. Resolution of severe ischemia-reperfusion injury post-lung transplantation after administration of endobronchial surfactant. *J Heart Lung Transplant.* 2007;26:850–6.
165. Samano MN, Minamoto H, Junqueira JJ, et al. Bronchial complications following lung transplantation. *Transplant Proc.* 2009;41:921–6.
166. Najafizadeh K, Daneshvar A, Dezfooli AA, et al. Pulmonary artery stenosis shortly after lung transplantation: successful balloon dilation and stent insertion in one case. *Ann Transplant.* 2009;14:52–5.
167. Husain S, Chan KM, Palmer SM, et al. Bacteremia in lung transplant recipients in the current era. *Am J Transplant.* 2006;6:3000–7.

168. Bonvillain RW, Valentine VG, Lombard G, et al. Post-operative infections in cystic fibrosis and non-cystic fibrosis patients after lung transplantation. *J Heart Lung Transplant*. 2007;26:890–7.
169. Campos S, Caramori M, Teixeira R, et al. Bacterial and fungal pneumonias after lung transplantation. *Transplant Proc*. 2008;40:822–4.
170. Mason DP, Marsh DH, Alster JM, et al. Atrial fibrillation after lung transplantation: timing, risk factors and treatment. *Ann Thorac Surg*. 2007;84:1878–84.
171. Barracough K, Menahem SA, Bailey M, et al. Predictors of decline in renal function after lung transplantation. *J Heart Lung Transplant*. 2006;25:1431–5.
172. Kahan ES, Petersen G, Gaughan JP, et al. High incidence of venous thromboembolic events in lung transplant recipients. *J Heart Lung Transplant*. 2007;26:339–44.
173. Bravo C, Gispert P, Borro JM, et al. Prevalence and management of gastrointestinal complications in lung transplant patients: MITOS study group. *Transplant Proc*. 2007;39:2409–12.
174. Hachem RR, Edwards LB, Yusen RD, et al. The impact of induction on survival after lung transplantation: an analysis of the International Society of Heart Lung Transplantation Registry. *Clin Transplant*. 2008;22:603–8.
175. Roithmaier S, Haydon AM, Loi S, et al. Incidence of malignancies in heart and/or lung transplant recipients: a single-institution experience. *J Heart Lung Transplant*. 2007;26:845–9.

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Key Points

- Chronic thromboembolic pulmonary hypertension results from repeated or unresolved emboli in the pulmonary circulation, and occurs in 3–4% of patients suffering acute pulmonary embolism.
- Pulmonary thromboendarterectomy is an endarterectomy of the entire pulmonary vascular tree, and is the preferred treatment for chronic thromboembolic pulmonary hypertension.
- The most common presenting symptom of chronic thromboembolic pulmonary hypertension is exertional dyspnea. The diagnosis is confirmed with echocardiography, right-sided cardiac catheterization, and pulmonary angiogram.
- Patients with chronic thromboembolic pulmonary hypertension, when left untreated, develop a small-vessel vasculopathy that mimics idiopathic pulmonary hypertension.
- Monitoring includes femoral and radial arterial pressures, processed EEG, pulmonary artery pressures, and transesophageal echocardiography.
- Anesthetic induction and maintenance are tailored to hemodynamic stability, right ventricular coronary perfusion pressure, and right ventricular support.
- Factors that lead to increased pulmonary vascular resistance, such as light anesthesia, acidosis, and hypoxemia, should be avoided.
- Pulmonary vasodilators such as nitric oxide and milrinone are generally ineffective in chronic thromboembolic pulmonary hypertension, but should be available for management of patients with small-vessel vasculopathy.

Introduction

Pulmonary thromboendarterectomy (PTE), a complete endarterectomy of the pulmonary vascular tree, is the definitive treatment for chronic thromboembolic pulmonary hypertension (CTEPH). Pulmonary embolism (PE) is a relatively common cardiovascular event, and in a small percentage of cases it leads to a chronic condition in which repeated microemboli as well as ongoing inflammatory response lead to accumulation of connective and elastic tissue on the surface of the pulmonary vessels.

Pulmonary thromboembolism is a significant cause of morbidity and mortality worldwide. Acute PE has been estimated to occur in approximately 63 per 100,000 patients per year in the United States with in-hospital mortality occurring in 11.1% [1]. These statistics probably represent underestimates, however, since in 70–80% of patients in whom the primary cause of death was PE, the diagnosis was unsuspected premortem [2]. If left untreated, the prognosis for patients with CTEPH is poor. In fact, once the mean pulmonary pressure in patients with CTEPH reaches 50 mmHg or more, the 3-year mortality approaches 90% [3]. Although medical management can provide temporary symptomatic relief, it is noncurative and generally ineffective. The only potentially curative options are lung transplantation and PTE, with PTE preferred because of its favorable long-term morbidity and mortality profile.

Although PTE is still uncommonly performed, increasing appreciation of CTEPH and recognition that PTE is the preferred treatment are resulting in an increase in interest in this operation. At this writing there have been over 2,000 PTEs

performed at UCSD. This chapter, based in large part on the experience at UCSD, provides a review of the natural history of CTEPH, a description of PTE, a discussion of anesthetic factors unique to PTE and CTEPH, and a case discussion on managing massive pulmonary hemorrhage, one of the feared complications of the operation.

Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Most cases of acute PE resolve within weeks and the patient recovers to their previous level of function. However, for unknown reasons, embolic resolution is sometimes incomplete. If the acute emboli are not lysed in 1–2 weeks, the embolic material becomes attached to the pulmonary arterial and arteriolar walls [4]. With time, the embolic material progressively becomes converted to connective and elastic tissue [5]. This chronic obstructive disease may lead to a small-vessel arteriolar vasculopathy characterized by excessive smooth muscle cell proliferation in pulmonary arterioles. This vasculopathy is seen in the remaining open vessels, which are subjected to long exposure to high flow and pressure. Pulmonary hypertension results from mechanical obstruction, as well as from this small-vessel vasculopathy. Once pulmonary hypertension has developed, patients require expeditious treatment. CTEPH patients generally do not respond well to medical management, which is reserved for patients who are not surgical candidates [6–8]. The only curative option is to proceed with surgical removal of the thromboembolic material by means of endarterectomy.

Incidence

The incidence of pulmonary hypertension caused by PE remains unknown. It has been estimated that there are more than 500,000 survivors of symptomatic episodes of acute PE per year [9]. One recent prospective study indicates that thromboembolic disease develops in as many as 3.8% of patients with acute PE [10]. Thus, a conservative estimate is that 19,000 individuals progress to CTEPH in the United States each year. Considering that only 200–300 PTEs are performed annually worldwide, it is clear that acute PE and CTEPH are under-diagnosed, and PTE is underutilized.

Etiologic Factors

No clear etiology has been defined for the development of CTEPH, although hypercoagulability is certainly a risk. Lupus anticoagulant may be detected in approximately 10% of chronic thromboembolic patients and 20% carry anticardiolipin antibodies, lupus anticoagulant, or both [11]. A recent study has demonstrated that the plasma level of factor VIII, a protein that is associated with both primary and recurrent venous thromboembolism, is elevated in 39% of patients with CTEPH. Analyses of plasma proteins in patients with chronic

thromboembolic disease have shown that fibrin from these patients is resistant to thrombolysis in vitro. In this study, the fibrin β chain N-terminus was particularly resistant to thrombolysis, suggesting that it could be responsible for thrombus nonresolution [12].

Case reports and anecdotal experience have suggested links between chronic thromboembolism and previous splenectomy, permanent intravenous catheters, and ventriculoatrial shunts for the treatment of hydrocephalus or chronic inflammatory conditions. In addition to these observations, associations with sickle cell disease, hereditary stomatocytosis, and the Klippel-Trenaunay syndrome have been described [13]. However, the vast majority of cases of CTEPH cannot be traced to a specific known coagulation defect or underlying medical condition.

Pathology and Pathogenesis

Although most individuals with CTEPH are unaware of a past thromboembolic or deep venous thrombosis, CTEPH likely stems from acute embolic episodes that do not completely resolve. Why some patients fail to resolve their emboli is unclear, but a variety of factors may play a role. The volume of acute embolic material may simply overwhelm the lytic mechanisms. The total occlusion of a major arterial branch may prevent lytic material from reaching, and therefore dissolving, the embolus completely. The emboli may be made of substances that cannot be lysed by normal mechanisms. These may include organized fibrous thrombus, fat, or tumor emboli; from stomach, breast, kidney, and right the right atrium (myxoma). The lytic mechanisms themselves may be abnormal, or some patients may have a hypercoagulable state. Hypercoagulability may result in spontaneous thrombosis within the pulmonary vascular bed, embolization, or lead to proximal propagation of embolic material. With time, the increased pressure and flow of redirected pulmonary blood flow in the previously normal pulmonary vascular bed can create a vasculopathy in the arterioles, similar to that of the Eisenmenger syndrome. This, as well as resulting right-sided heart failure can lead to an inoperable, lethal situation, so early surgical intervention is recommended.

Clinical Presentation

The most common symptom of CTEPH, as with pulmonary hypertension in general, is exertional dyspnea. This dyspnea is out of proportion to abnormalities found on clinical examination. Syncope is another common symptom of pulmonary hypertension, particularly in patients with advanced disease. Other common findings include chest tightness, hemoptysis, peripheral edema, and early satiety.

The physical signs of pulmonary hypertension are the same regardless of the underlying pathophysiology. Jugular venous distension is common, with prominent the V-waves. The right ventricle is usually palpable near the lower left sternal border, and pulmonary valve closure may be audible in the second intercostal space. Patients with advanced disease

may be cyanotic. A systolic murmur characteristic of tricuspid regurgitation is common, and murmurs over the lung fields resulting from turbulent flow in the pulmonary vessels may also be appreciated.

Workup may include chest radiograph (CXR), pulmonary function testing, right heart catheterization with pulmonary angiography, high-resolution magnetic resonance imaging, arterial blood gas analysis, ventilation/perfusion scanning, and echocardiography. CXR may show lung opacities suggestive of previous scarring, hyperlucent areas suggestive of regional decreased blood flow, right-sided cardiomegaly, and dilatation of the pulmonary vessels (Fig. 38.1). Diffusing capacity

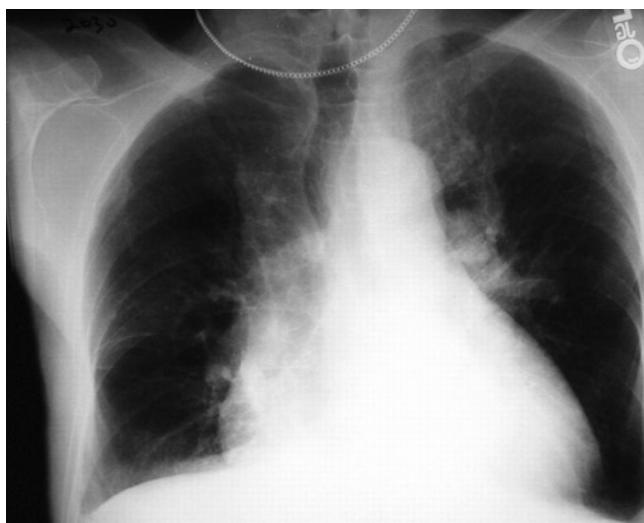


FIG. 38.1. Chest radiograph of a patient with advanced chronic thromboembolic pulmonary hypertension. Cardiomegaly, hilar fullness, and decrease in vascularity in areas of the lung fields are apparent.

(DLCO) is often reduced and may be the only abnormality on pulmonary function testing. Pulmonary arterial pressure is elevated, sometimes being supra-systemic. Resting cardiac output is often low, with reduced pulmonary arterial oxygen saturation. Many patients exhibit hypoxia, particularly with exercise; room air arterial oxygen tension ranges between 50 and 83 torr, the average being 65 torr [14]. CO_2 tension is often slightly reduced, although dead space ventilation is increased. Ventilation–perfusion studies show moderate mismatch, but correlate poorly with the degree of pulmonary vascular obstruction [15].

Transthoracic echocardiography is often the first study to provide clear evidence of pulmonary hypertension. An estimate of pulmonary artery systolic pressure is often provided by Doppler of the tricuspid regurgitant envelope. Echocardiographic findings vary depending on the stage of the disease and include right ventricular enlargement, leftward displacement of the interventricular septum, and encroachment of the enlarged right ventricle on the left ventricular cavity with abnormal systolic and diastolic function of the left ventricle. Thankfully, many of these abnormalities resolve after successful PTE [16]. Contrast echocardiography may demonstrate a persistent foramen ovale, the result of high right atrial pressures opening the previously closed intraatrial communication.

Pulmonary angiography is the gold standard for defining pulmonary vascular anatomy and is performed to confirm the diagnosis and to determine the location and surgical accessibility of thromboembolic disease. In angiographic imaging, thrombi appear as unusual filling defects, pouches, webs, or bands, or completely thrombosed vessels that may resemble congenital absence of a vessel (Fig. 38.2). More recently, high-resolution computed tomography scanning [17], SPECT-CT

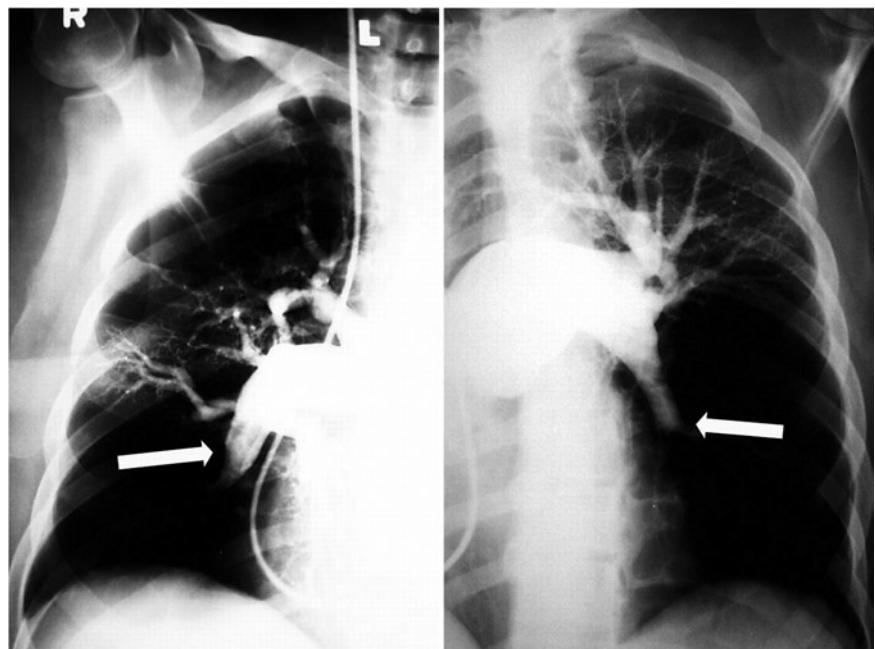


FIG. 38.2. Pulmonary angiogram showing perfusion defects (arrows) and large hyperlucent areas resulting from pulmonary vascular obstruction.

fusion imaging [18], and magnetic resonance angiography [19] have been used successfully to screen patients with suspected thromboembolic disease.

In approximately 10% of cases, the differential diagnosis between primary pulmonary hypertension and distal and small-vessel pulmonary thromboembolic disease remains unclear and hard to establish. In these patients, pulmonary angioscopy is often helpful. The pulmonary angioscope is a fiberoptic scope that is placed through a central line into the pulmonary artery. The tip contains a balloon that is then filled with saline and pushed against the vessel wall. A bloodless field can thus be obtained to view the pulmonary artery wall. The classic appearance of chronic pulmonary thromboembolic disease by angioscopy consists of intimal thickening, with intimal irregularity and scarring, and webs across small vessels. The presence of embolic disease, occlusion of vessels, or the presence of thrombotic material is diagnostic [5].

Many CTEPH patients have longstanding pulmonary hypertension; as many as 37% of them receive medical pulmonary vasodilator therapy [20]. This therapy may consist of phosphodiesterase 5 inhibition (e.g., sildenafil) [21], endothelin-1 inhibition (e.g., bosentan) [22, 23], and prostacyclin analogs (e.g., iloprost, flolan, remodulin) [24–26]. It is prudent to continue these medications preoperatively and to consider their use postoperatively if the surgical result is suboptimal. Abrupt cessation of a prostacyclin analog can result in potentially catastrophic rebound pulmonary hypertension [27]. If a patient presents with an epoprostenol (Flolan™) infusion, one approach is to continue this infusion throughout the pre-CPB period, discontinue it during CPB, and restart it after CPB if the surgical result is suboptimal. If the surgical result is good, keep it available to be restarted if pulmonary hypertension develops postoperatively.

The Surgical Procedure

Surgical Approach and Technique

PTE, being an endarterectomy of the entire pulmonary vascular tree, is performed through a midline sternotomy, and requires cardiopulmonary bypass (CPB) with deep hypothermic circulatory arrest (DHCA). Although used in the past, lateral thoracotomy is suboptimal [28]. Median sternotomy allows treatment of both pulmonary arteries, which is necessary in almost all cases [28, 29]. The use of CPB with periods of complete circulatory arrest provides the bloodless operative field necessary for complete meticulous lobar and segmental dissections [30].

Following median sternotomy, CPB is established with cannulation of the ascending aorta and the inferior and superior vena cava. Cooling is instituted immediately. A gradient of not more than 10°C is maintained between the arterial blood and the bladder/rectal temperature. This allows an even distribution of cooling and warming, as well as helping to prevent release

of gas bubbles into the circulation upon rewarming. Pulmonary artery and pulmonary venous vents are inserted. During the cooling phase venous oxygen saturation increases, with a saturation of 80% typical at 25°C, and 90% at 20°C. Hemodilution to a hematocrit of 18–25% is utilized to decrease blood viscosity, optimize capillary blood flow, and promote uniform cooling. Complete cooling typically requires 45–60 min, depending on the size and perfusion characteristics of the patient.

As core temperature approaches 20°C and tympanic membrane temperature approaches 16–18°C, the aorta is cross-clamped. Immediately after aortic cross-clamping, cardioplegia solution is administered into the aortic root. Additional myocardial protection is afforded by a circulating cold water cooling jacket around the heart. An incision is made in the right pulmonary artery with the surgeon standing on the patient's left. The right pulmonary artery endarterectomy plane is established and dissection continues until bronchial artery flow impairs good visualization. At this point circulatory arrest is imperative. Bronchial flow in these patients is frequently substantial and without circulatory arrest complete endarterectomy cannot be accomplished.

Circulatory arrest is limited to 20-min epochs. An experienced surgeon can usually accomplish the entire unilateral endarterectomy within this time period. If additional arrest time is necessary, reperfusion is carried out at 18°C core temperature for a minimum of 10 min. At the completion of the endarterectomy, perfusion is re-established while the pulmonary artery incision is closed.

Following a 10-min period of hypothermic perfusion, the left pulmonary artery is incised and an endarterectomy is performed. Following completion of the left endarterectomy, a patent foramen ovale (PFO), if present, is repaired. Any additional procedures such as coronary artery bypass grafting or valve replacement can be performed during the rewarming period.

Surgical Subtypes

There are four types of pulmonary occlusive disease [27, 34, 35]. In Type 1 (38% of cases), a major vessel clot is present and readily visible on the opening of the pulmonary arteries (Fig. 38.3). In Type 2 (42% of cases), no major vessel thrombus can be appreciated, but thickened intima (fibrous connective tissue) is present throughout much of the vasculature (Fig. 38.4). Type 3 disease (18% of cases) is similar to Type 2 but very distal (Fig. 38.5). Type 4 does not represent primary thromboembolic pulmonary hypertension and is inoperable.

Anesthetic Management

Setup, Preparation

A typical “setup” for a pulmonary endarterectomy includes preparation for transesophageal echocardiography (TEE), pulmonary artery catheterization, hemodynamic support, cerebral

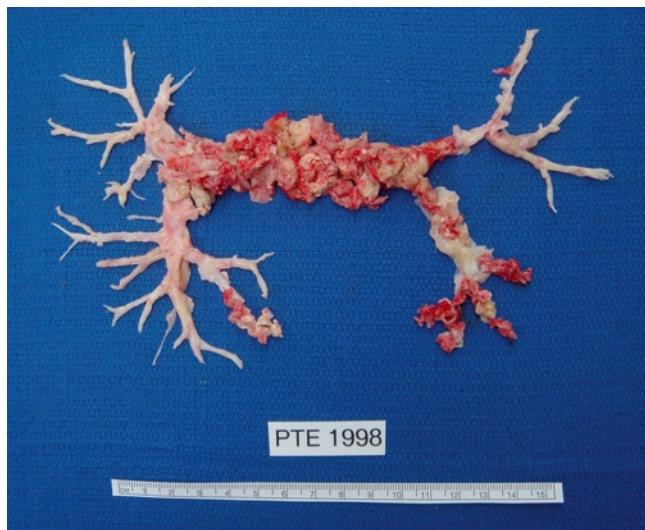


FIG. 38.3. Endarterectomy specimen of Type 1 thromboembolic disease. Thrombus and fibrous connective tissue were removed from much of the pulmonary vascular tree.



FIG. 38.5. Endarterectomy specimen of Type 3 thromboembolic disease. Only distal fibrous connective tissue was found at surgery.

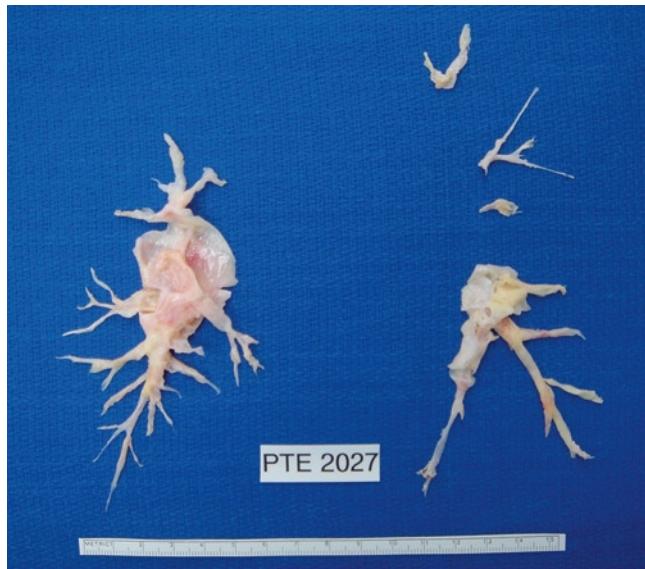


FIG. 38.4. Endarterectomy specimen of Type 2 thromboembolic disease. Fibrous connective tissue was removed from much of the pulmonary vascular tree.

function monitoring, and a cooling device for head cooling. On the day of surgery, a large bore peripheral intravenous catheter and a radial arterial catheter are inserted. The patient may then be given light sedation (with caution) and brought to the operating room. Even small amounts of sedation may cause respiratory depression, leading to a catastrophic rise in pulmonary vascular resistance. Supplemental oxygen should be considered in the preoperative area, particularly if sedation is administered.

Anesthetic Induction and Pre-CPB Management

After thorough preoxygenation and ventilation encouragement, anesthetic induction can be accomplished with midazolam, fentanyl, and a muscle relaxant. Myocardial depressants such as propofol should be used with extreme caution, if at all. In cases of tenuous hemodynamics, etomidate may be useful because of its relative lack of cardiovascular depression. A pulmonary artery catheter is generally placed after induction rather than before, since the hemodynamic status and goals are usually known by the time the patient reaches the operating room. Also, lying awake in the supine or Trendelenberg position may be stressful for patients with advanced disease, occasionally leading to cardiorespiratory instability. If preoperative transthoracic echocardiography shows evidence of right atrial or right ventricular thrombi, TEE is performed immediately after induction, prior to placement of a pulmonary artery catheter.

Although some patients with CTEPH presenting for pulmonary endarterectomy have associated left ventricular pathology, most do not. Hemodynamic management is thus centered on right ventricular function. The right ventricle is usually hypertrophic and dilated, as is the right atrium. Because of the high right-sided pressures, the coronary blood supply to right ventricle is at risk. Maintenance of adequate systemic vascular resistance (SVR), inotropic state, and normal sinus rhythm serve to preserve systemic hemodynamics as well as right ventricular coronary perfusion. The preoperative cardiac catheterization data, including cardiac output, pulmonary vascular resistance (PVR), patency of coronary arteries, and right ventricular end-diastolic pressure (RVEDP) are useful in planning the induction sequence. Elevated RVEDP

(>14 mmHg), severe tricuspid regurgitation, and preoperative PVR>1,000 dyne-s-cm⁻⁵ are signs of impending decompensation. In such cases inotropic support (e.g., dopamine or epinephrine), as well as vasopressor support (e.g., phenylephrine or vasopressin) should be considered for the induction and pre-CPB period. Generally, patients with CTEPH have fixed PVR because of mechanical obstruction. However, high PVR can still be exacerbated by factors that increase PVR (e.g., hypoxia, hypercarbia, acidosis, pain, and anxiety). Thus, these stressors should be minimized during induction and immediate pre-CPB period. Attempts to lower the PVR pharmacologically (e.g., nitroglycerin, nitroprusside) should be avoided as they have minimal efficacy in treating CTEPH and can dangerously jeopardize the coronary perfusion pressure to the right ventricular myocardium. This can rapidly lead to hypotension and cardiovascular collapse. Direct pulmonary vasodilators such as nitric oxide and prostaglandins, which may be useful in the medical management of patients with other types of pulmonary hypertension, generally show limited benefit for pulmonary endarterectomy patients in the perioperative period. The effects of phenylephrine on right ventricular performance in pulmonary hypertension has been studied by Rich et al. [31]. They documented improved right ventricular performance (increased MAP, coronary artery perfusion pressure, maintained cardiac output) with phenylephrine administration. Since hemodynamic collapse can occur very rapidly in these patients, it is particularly important to treat decreases in blood pressure and heart rate rapidly and aggressively. The muscle relaxant is chosen according to airway issues and desired hemodynamic response. Pancuronium, rocuronium, and vecuronium have all been used successfully in these patients.

If the superior vena cava is patent, an internal jugular introducer and pulmonary artery catheter are inserted. Placement of the pulmonary artery catheter may be difficult because of right atrial and right ventricular dilatation, as well as tricuspid regurgitation and pulmonary artery pathology. If it cannot be placed in the pulmonary artery, it is left in the superior vena cava (about 20 cm) and an attempt is made later under echocardiographic or surgical guidance.

Next, a femoral arterial catheter is placed. This is because, in cases involving prolonged hypothermic CPB, the systemic arterial pressure is significantly underestimated by the radial artery catheter in the post-CPB period [32]. This phenomenon has been noticed by others [33], and appears to be accentuated by prolonged periods of profound hypothermia. It is not uncommon for a mean arterial pressure (MAP) gradient of as much as 20 mmHg to develop after CPB. The mechanism is unclear; causes involving peripheral vasoconstriction and vasodilatation have been proposed [33, 34]. Although the time course for recovery of the radial arterial wave is variable, typically the radial and femoral pressure measurements show reasonable agreement by the morning following surgery [32].

TEE is valuable in monitoring and assessing cardiac function and filling during PTE. The most useful views include the

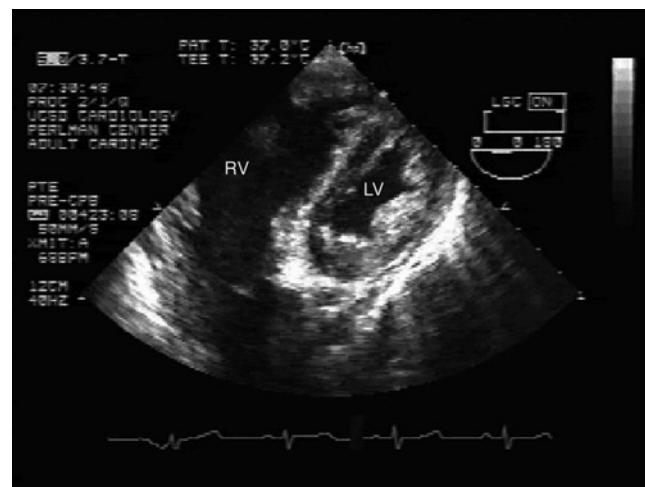


FIG. 38.6. Transgastric short-axis transesophageal echocardiograph in a PTE patient with massively enlarged right ventricle. *RV* right ventricle; *LV* left ventricle.



FIG. 38.7. Modified (slightly deeper, showing coronary sinus) four-chamber transesophageal echocardiograph in a PTE patient with severe right ventricular hypertrophy, and enlarged right ventricle and coronary sinus. *RV* right ventricle; *RA* right atrium; *LV* left ventricle; *CS* coronary sinus.

transgastric mid short-axis view to assess left ventricular size and septal motion (Fig. 38.6), the mid esophageal four-chamber view for relative chamber sizes, intracardiac thrombus, and tricuspid valve assessment (Fig. 38.7), the mid esophageal bicaval view (interatrial septal integrity, thrombosis of the great veins), and the mid esophageal aortic short-axis view for size of the pulmonary artery (PA), and detecting PA thrombus. It is not uncommon to find substantial dilatation of the PA, as well as thromboembolic material (Fig. 38.8). The integrity of the interatrial septum is investigated with the use of an agitated saline test. PFO is present in 25–35% of PTE patients [35]. If a PFO is present, it is repaired, since, postoperatively some patients may experience high right-sided pressures. Such pressures, in the presence of a PFO, could lead to right-to-left shunt and hypoxemia.

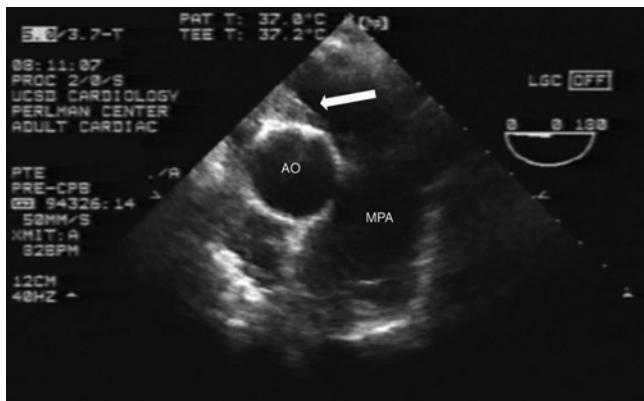


FIG. 38.8. Mid esophageal aortic short-axis transesophageal echocardiograph showing dilatation of the main pulmonary artery and thromboembolic material at the origin of the right pulmonary artery (arrow). MPA main pulmonary artery; AO aorta.

Processed electroencephalogram (EEG) is monitored throughout the procedure. This allows confirmation of minimal oxygen utilization of the brain prior to circulatory arrest (isoelectric EEG), as well as monitoring of level of consciousness during normothermia. In our institution the “Sedline” monitor (Hospira, Lape Forest, IL) is used because of its superior waveform display, although the “Bis monitor” (Aspect Medical, Inc., Newton, MA) has also been used with success. Temperature monitoring is done with a urinary catheter with temperature monitoring capabilities, a rectal probe, and tympanic membrane probe, which provides an estimation of brain temperature [36]. The rectal and bladder probes estimate core temperature, and the PA catheter measures blood temperature, allowing quantification of thermal gradients.

If the hematocrit and hemodynamics permit, 1–2 units of autologous blood are harvested for reinfusion after CPB.

During the precardiopulmonary bypass period, the head is wrapped in a circulating cold-water blanket. The water, maintained at 4°C, is circulated through the blanket by an electric pump. This system (Polar Care, Breg, Inc., Vista, CA), originally designed as a “knee-wrap” for orthopedic and physical medicine purposes, is easily applied to the head. It contains a thermometer within the fluid circulation system for confirmation of adequate blanket cooling, as well as a flow control dial. This head-wrap is used in all PTEs at UCSD, with no complications. It is our belief that the blanket provides better cooling to the surface of the cranium, particularly posterior regions, than application of ice bags, and is easier to apply.

Another consideration is prior exposure and response to heparin. Because of prior exposure, some patients develop heparin-induced antiplatelet antibodies, causing a propensity to heparin-induced thrombocytopenia. Anticoagulation for these patients has been managed with preheparin administration of iloprost (a prostacyclin analog), heparinoid [29, 30], hirudin, and bivalirudin [37, 38]. Most recently, we have had success using the platelet inhibitor tirofiban [39, 40].

Management of Deep Hypothermic Circulatory Arrest (DHCA)

Prior to DHCA mannitol (12.5 g), methylprednisolone sodium succinate (30 mg/kg), phenytoin sodium (15 mg/kg), and sodium thiopental (6 mg/kg) are administered. Mannitol is used to promote an osmotic diuresis, minimize cellular edema, and for free radical scavenging. Methylprednisolone theoretically functions as a cell-membrane stabilizer and anti-inflammatory agent. Phenytoin may provide some protection against postoperative seizures, and sodium thiopental may provide some cerebral protection. Interestingly, thiopental causes vasoconstriction when the patient is deeply hypothermic, and CPB flow may need to be decreased temporarily to prevent hypertension [41]. While there is no clear clinical evidence supporting added benefit of barbiturate administration for DHCA, we give thiopental for three reasons: (1) brain cooling may be uneven or incomplete, (2) cerebral emboli may occur during rewarming (pulmonary endarterectomy is an “open-chamber” procedure), (3) even at 18°C we often notice sparse EEG activity which is then abolished with administration of thiopental.

After assurance of an isoelectric EEG and tympanic membrane temperature 18°C or less, circulatory arrest is instituted. At this time, all monitoring lines are turned off to the patient, decreasing the risk of entraining air into the vasculature during exsanguination.

Monitoring jugular venous bulb oxygen saturation may be useful in detecting adverse cerebral effects of rapid warming [42], or for prognosticating postoperative neurologic function [43]. However, since our warming rate is slow, and our neurologic results are good, we choose not to expose our patients to the added risks of jugular venous bulb catheterization. Surface cerebral oximetry is a noninvasive technique applying near-infrared spectroscopy to measure hemoglobin oxygen saturation in the brain underlying the sensor. The number reported by the monitor is rSO₂, which is a measure of the mixed arterial and venous blood in the brain. Since venous blood volume accounts for 70–90% of total cerebral blood volume, rSO₂ reflects oxygen saturation of venous blood and thus the relationship between cerebral oxygen metabolism (demand) and cerebral blood flow (supply). In healthy volunteers, rSO₂ has been found to correlate with jugular venous saturation [44, 45], although, during cardiac surgery the correlation between the two monitors is not always close [46]. Ongoing research in this area and additional neuropsychiatric outcome studies may prove this monitor useful during the conduct of DHCA.

Post-DHCA Rewarming

A 10° gradient between blood and bladder/rectal temperature is not exceeded during rewarming, and the perfusate temperature is never greater than 37.5°. Warming too quickly promotes systemic gas bubble formation, cerebral oxygen desaturation, and uneven warming. Rewarming times are variably related to

the patient's weight and systemic perfusion; 90–120 min are usually required to achieve a core temperature of 36.5°C.

Separation from CPB

With the following few exceptions, the process of separation from CPB is similar to other surgeries involving CPB. End-tidal carbon dioxide (ETCO₂) is a poor measure of ventilation adequacy in these patients both pre- and post-CPB, since dead space ventilation is an integral part of the disease process. After successful surgery, the arterial-ETCO₂ gradient may be decreased compared to preoperative values, but the time course for this improvement is variable. While still on CPB, the TEE is used to detect intracavitory air as well as to evaluate left and right ventricular function. The anesthesiologist checks the endotracheal tube for frothy sputum or bleeding because reperfusion pulmonary edema and airway bleeding, two of the most dreaded complications of the procedure, may manifest at this time [47].

For separation from CPB, modest inotropic support (e.g., dopamine, 3–7 µg/kg/min) is often necessary because of the long hypothermic period and long aortic cross-clamp time. In patients with particularly poor ventricular function epinephrine 0.04–0.15 µg/kg/min is added. If the surgery has only been partially successful because of small-vessel disease, pulmonary vasodilators such as milrinone, inhaled prostacycline, and nitric oxide are considered. If the surgery has been successful, the TEE reveals immediate improvements in the left- and right-sided geometry [48, 49]. The distention of the right atrium and right ventricle is greatly decreased, resulting in improvement of function of both ventricles. Tricuspid regurgitation, if it was present before the endarterectomy, has greatly decreased or resolved. Significant improvement in hemodynamic status is usually noted, including a doubling of the cardiac index, dramatic decrease in PA pressures, and a drop in the PVR to 25% of the preoperative value [50].

Post-CPB Management

Frothy sputum, if present, likely indicates the onset of reperfusion pulmonary edema. In this case, the endotracheal tube is suctioned and increasing amounts of positive end-expiratory pressure (PEEP) are applied beginning with 5 cmH₂O escalating to 7.5 and 10 cmH₂O. If frank blood is emanating from the endotracheal tube, surgical bleeding is the probable culprit. PEEP is increased and aggressive suctioning of the blood is undertaken. If severe bleeding persists, fiberoptic bronchoscopy is used to evaluate the source of bleeding and lung isolation maneuvers (bronchial blocker, double lumen endobronchial tube) are considered. Topical vasopressors such as vasopressin and epinephrine, administered via the endotracheal tube, may also be useful [47].

After heparin reversal, bleeding diathesis is rare, and transfusion requirements are usually minimal [50]. Antifibrinolytic agents such as ϵ -amino-caproic acid and aprotinin are not routinely used for pulmonary endarterectomy in our institution.

Postoperative Management

Two major postoperative complications unique to PTE are reperfusion pulmonary edema and pulmonary arterial steal. Reperfusion pulmonary edema is a localized form of high-permeability (noncardiogenic) lung injury, a form of adult respiratory distress syndrome, localized to the area of lung having received the endarterectomy. It usually occurs within the first 24 h but may appear up to 72 h following PTE [51]. In most cases it is mild; reperfusion edema resulting in clinically significant morbidity occurs in only 10% of cases. In its most severe form, it begins immediately post-CPB, in the operating room as described above. These patients are often extremely ill, requiring aggressive intensive care and ventilator management. Pressure control, PEEP, and inverse ratio ventilation are used judiciously in an effort to improve V/Q matching and minimize further pulmonary injury. Occasionally extracorporeal support is required [52, 53]. Pulmonary arterial steal represents a postoperative redistribution of pulmonary arterial blood away from the previously well-perfused segments into the newly endarterectomized segments [54]. Whether the cause is failure of autoregulation in the newly endarterectomized segments or secondary small-vessel changes in the previously open segments has not been clarified. However, long-term follow-up has documented a decrease in pulmonary vascular steal in the majority of patients, suggesting a remodeling process in the pulmonary vascular bed [55].

Other postoperative complications are rare, but can include pulmonary hemorrhage (0.4%), neurologic sequelae (0.4%), mediastinal bleeding (3.5%), GI bleeding (1.6%), atrial fibrillation (2.6%), renal failure requiring renal replacement therapy (1%), and sepsis (1.2%) [56].

PTE patients usually awaken within 1–2 h after surgery, and a brief neurologic examination is performed. The patient is then sedated with a propofol infusion and analgesics. They remain intubated over night, since the onset of reperfusion pulmonary edema may be delayed. If pulmonary, cardiac, and neurologic function is good, and there is no bleeding diathesis, extubation occurs the following morning. Discharge from the intensive care unit typically occurs on the second or third postoperative day, and the patients are usually discharged from the hospital 1 week after the operation.

Outcome After PTE

There has been steady improvement in mortality rate at UCSD since 1980, with current perioperative mortality rate being less than 3% (Fig. 38.9). We believe these results from improvements in preoperative preparation, surgical technique, anesthetic care, perfusion technique, and postoperative management. The positive effect of experience, in the form of case volume, on outcome has been well documented for other types of complicated surgery, such as liver transplantation [57]. In addition, we have developed close collaboration between the Pulmonary Medicine, Cardiac Surgery, and Anesthesiology.

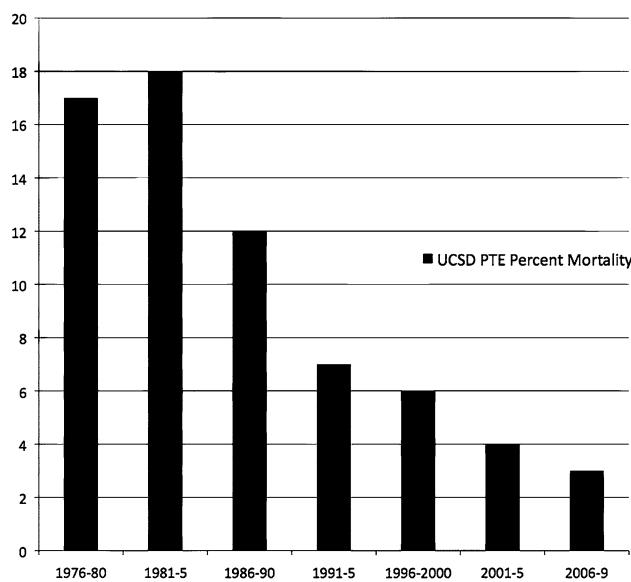


FIG. 38.9. Bar graph showing progressive improvement in perioperative mortality at UCSD over the past 33 years. Year intervals are on the X-axis, percentage mortality on the Y-axis.

This “team approach,” we believe, is absolutely essential to a successful PTE program.

With this operation, a reduction in pulmonary pressures and resistance to normal levels and corresponding improvement in pulmonary blood flow and cardiac output are generally immediate and sustained [56, 58, 59]. Mortality rate and improvements in hemodynamics depend heavily on surgical subtype, with Type 1 and 2 fairing better than Type 3. Type 4, not being CTEPH but rather small-vessel disease, is associated with poor outcome (Table 38.1) [56]. Patients who have undergone a successful PTE enjoy long-term benefit. Typically patients preoperatively present as New York Heart Association (NYHA) class III or IV, and often maintain NYHA I and II function indefinitely following the operation [60].

TABLE 38.1. Acute changes in hemodynamics by surgical subtype and associated mortality statistics for 1,100 UCSD PTE patients immediately prior to 2008.

Variable	All patients (n=1,100, 100%)	Type 1 (n=415, 37.7%)	Type 2 (n=469, 42.6%)	Type 3 (n=192, 17.5%)	Type 4 (n=24, 2.2%)
PVR(dynes-sec-cm ⁻⁵)	859.4±439.5 290.4±195.7	924.2±450.4 269.8±176.6	799.9±417.2 270.5±191.3	863.2±454.6 350.8±183.3	884.6±412.3 595.2±360.2
CO(L/min)	3.9±1.3 5.4±1.5	3.7±1.4 5.5±1.5	4.1±1.3 5.5±1.5	4.0±1.5 5.2±1.4	3.8±1.2 4.5±1.1
Systolic PA pressure(mmHg)	75.9±18.6 46.4±16.6	76.8±18.7 44.4±15.1	75.0±19.5 44.5±15.0	75.8±16.4 52.7±17.1	78.4±15.6 73.8±32.1
Diastolic PA pressure (mmHg)	28.5±9.7 18.5±7.2	29.8±9.6 17.7±6.5	27.3±10.0 17.9±6.8	28.3±8.8 20.6±7.9	32.3±9.5 27.3±12.8
Mean PA pressure (mmHg)	46.2±11.3 28.4±9.6	47.0±11.4 27.2±8.7	45.2±11.6 27.5±9.1	46.5±10.3 31.8±10.1	50.2±10.5 42.4±15.5
Mortality (%)	52 (4.7)	16 (3.9)	22 (4.7)	12 (6.3)	4 (16.7)

Data shown as means±standard deviation or numbers (percentage). Top numbers are preoperative, bottom numbers from pulmonary artery catheter immediately prior to removal in ICU

PVR pulmonary vascular resistance; CO cardiac output; PA pulmonary artery

Reprinted with permission from Thistlethwaite et al. [56]

Future

There remain many unanswered questions about CTEPH and PTE. Research to determine the etiology of CTEPH, as well as the mechanisms and factors leading to reperfusion pulmonary edema, vascular steal, and ischemic neurologic injury continues. Understanding these processes will most likely lead to improved prophylaxis and treatment. Anesthesiologists, in particular, will be an integral part of future research on the immediate perioperative period. This will include efforts to improve the management of residual “small-vessel disease,” right ventricular failure, cerebral function and oxygenation monitoring, postoperative pulmonary edema, pulmonary bleeding, and organ protection.

Clinical Case Discussion

Case: A 68-year-old woman with CTEPH underwent a PTE, and has just been separated from CPB. The surgeon tells you that the endarterectomy was difficult because it was Type 3 disease and the thromboembolic material was particularly “sticky.” You suspected such because the surgeon required two circulatory arrests on the right side, and he usually requires only one on each side. Large amounts of dark blood appear in the endotracheal tube as you begin ventilating.

Questions

- What is the most likely cause of this bleeding?
- What diagnostic maneuvers can be performed to determine the cause and location of the bleeding?
- What are the therapeutic options, and how will they be chosen?

The most likely cause is surgical trauma; puncture of the distal pulmonary arteries resulting from aggressive endarterectomy.

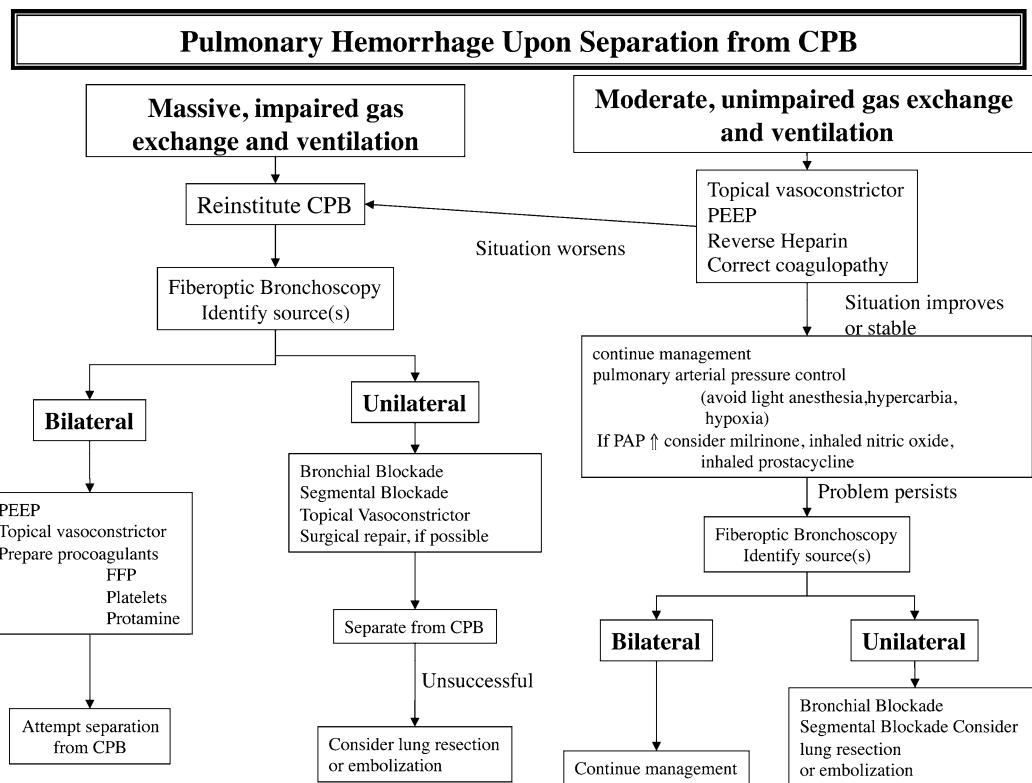


FIG. 38.10. Algorithm for management of post-CPB pulmonary bleeding (Manecke et al. [47]).

Other possibilities include nonsurgical PA rupture (high pressure, PA catheter trauma). Diagnosis and treatment are similar to other cases of pulmonary hemorrhage. Diagnosis and localization are based on fiberoptic bronchoscopy findings, and choice of treatment (e.g., lung isolation, PEEP, topical vasoconstrictors such as vasopressin, phenylephrine) depends on the severity of the bleeding. An algorithm for management of post-CPB hemorrhage is presented in Fig. 38.10.

References

1. DeMonaco NA, Dang Q, Kapoor WN, Ragni MV. Pulmonary embolism incidence is increasing with use of spiral computed tomography. *Am J Med.* 2008;121(7):611–7.
2. Lindblad B, Eriksson A, Bergqvist D. Autopsy-verified pulmonary embolism in a surgical department: analysis of the period from 1951 to 1988. *Br J Surg.* 1991;78(7):849–52.
3. Riedel M, Stanek V, Widimsky J, Prerovsky I. Longterm follow-up of patients with pulmonary thromboembolism. Late prognosis and evolution of hemodynamic and respiratory data. *Chest.* 1982;81(2):151–8.
4. Bernard J, Yi ES. Pulmonary thromboendarterectomy: a clinicopathologic study of 200 consecutive pulmonary thromboendarterectomy cases in one institution. *Hum Pathol.* 2007;38(6):871–7.
5. Guillinta P, Peterson KL, Ben-Yehuda O. Cardiac catheterization techniques in pulmonary hypertension. *Cardiol Clin.* 2004;22(3):401–15. vi.
6. Post MC, Plokker HW, Kelder JC, Snijder RJ. Long-term efficacy of bosentan in inoperable chronic thromboembolic pulmonary hypertension. *Neth Heart J.* 2009;17(9):329–33.
7. Vassallo FG, Kodric M, Scarduelli C, et al. Bosentan for patients with chronic thromboembolic pulmonary hypertension. *Eur J Intern Med.* 2009;20(1):24–9.
8. Jais X, D'Armini AM, Jansa P, et al. Bosentan for treatment of inoperable chronic thromboembolic pulmonary hypertension: BENEFiT (Bosentan Effects in iNopErable Forms of chronic Thromboembolic pulmonary hypertension), a randomized, placebo-controlled trial. *J Am Coll Cardiol.* 2008;52(25):2127–34.
9. Dalen JE, Alpert JS. Natural history of pulmonary embolism. *Prog Cardiovasc Dis.* 1975;17(4):259–70.
10. Pengo V, Lensing AW, Prins MH, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. *N Engl J Med.* 2004;350(22):2257–64.
11. Fedullo PF, Auger WR, Kerr KM, Rubin LJ. Chronic thromboembolic pulmonary hypertension. *N Engl J Med.* 2001;345(20):1465–72.
12. Bonderman D, Turecek PL, Jakowitsch J, et al. High prevalence of elevated clotting factor VIII in chronic thromboembolic pulmonary hypertension. *Thromb Haemost.* 2003;90(3):372–6.
13. Lang IM. Chronic thromboembolic pulmonary hypertension—not so rare after all. *N Engl J Med.* 2004;350(22):2236–8.
14. Kapitan KS, Buchbinder M, Wagner PD, Moser KM. Mechanisms of hypoxemia in chronic thromboembolic pulmonary hypertension. *Am Rev Respir Dis.* 1989;139(5):1149–54.
15. Moser KM, Daily PO, Peterson K, et al. Thromboendarterectomy for chronic, major-vessel thromboembolic pulmonary hypertension.

- Immediate and long-term results in 42 patients. *Ann Intern Med.* 1987;107(4):560–5.
16. D'Armini AM, Zanotti G, Ghio S, et al. Reverse right ventricular remodeling after pulmonary endarterectomy. *J Thorac Cardiovasc Surg.* 2007;133(1):162–8.
17. Reichelt A, Hooper MM, Galanski M, Keberle M. Chronic thromboembolic pulmonary hypertension: evaluation with 64-detector row CT versus digital subtraction angiography. *Eur J Radiol.* 2009;71(1):49–54.
18. Suga K, Kawakami Y, Iwanaga H, Hayashi N, Seto A, Matsunaga N. Comprehensive assessment of lung CT attenuation alteration at perfusion defects of acute pulmonary thromboembolism with breath-hold SPECT-CT fusion images. *J Comput Assist Tomogr.* 2006;30(1):83–91.
19. Nikolaou K, Schoenberg SO, Attenberger U, et al. Pulmonary arterial hypertension: diagnosis with fast perfusion MR imaging and high-spatial-resolution MR angiography—preliminary experience. *Radiology.* 2005;236(2):694–703.
20. Jensen KW, Kerr KM, Fedullo PF, et al. Pulmonary hypertensive medical therapy in chronic thromboembolic pulmonary hypertension before pulmonary thromboendarterectomy. *Circulation.* 2009;120(13):1248–54.
21. Archer SL, Michelakis ED. Phosphodiesterase type 5 inhibitors for pulmonary arterial hypertension. *N Engl J Med.* 2009;361(19):1864–71.
22. Rubin LJ, Badesch DB, Barst RJ, et al. Bosentan therapy for pulmonary arterial hypertension. *N Engl J Med.* 2002;346(12):896–903.
23. Confalonieri M, Kodric M, Longo C, Vassallo FG. Bosentan for chronic thromboembolic pulmonary hypertension. *Expert Rev Cardiovasc Ther.* 2009;7(12):1503–12.
24. Vizza CD, Badagliacca R, Sciomer S, et al. Mid-term efficacy of beraprost, an oral prostacyclin analog, in the treatment of distal CTEPH: a case control study. *Cardiology.* 2006;106(3):168–73.
25. Ono F, Nagaya N, Okumura H, et al. Effect of orally active prostacyclin analogue on survival in patients with chronic thromboembolic pulmonary hypertension without major vessel obstruction. *Chest.* 2003;123(5):1583–8.
26. Nagaya N, Sasaki N, Ando M, et al. Prostacyclin therapy before pulmonary thromboendarterectomy in patients with chronic thromboembolic pulmonary hypertension. *Chest.* 2003;123(2):338–43.
27. Augoustides JG, Culp K, Smith S. Rebound pulmonary hypertension and cardiogenic shock after withdrawal of inhaled prostacyclin. *Anesthesiology.* 2004;100(4):1023–5.
28. Jamieson SW. Pulmonary thromboendarterectomy [editorial]. *Heart.* 1998;79(2):118–20.
29. Fedullo PF, Auger WR, Channick RN, Moser KM, Jamieson SW. Chronic thromboembolic pulmonary hypertension. *Clin Chest Med.* 1995;16(2):353–74.
30. Jamieson SW, Auger WR, Fedullo PF, et al. Experience and results with 150 pulmonary thromboendarterectomy operations over a 29-month period. *J Thorac Cardiovasc Surg.* 1993;106(1):116–26. discussion 126–117.
31. Rich S, Gubin S, Hart K. The effects of phenylephrine on right ventricular performance in patients with pulmonary hypertension. *Chest.* 1990;98(5):1102–6.
32. Manecke Jr GR, Parimucha M, Stratmann G, et al. Deep hypothermic circulatory arrest and the femoral-to-radial arterial pressure gradient. *J Cardiothorac Vasc Anesth.* 2004;18(2):175–9.
33. Mohr R, Lavee J, Goor DA. Inaccuracy of radial artery pressure measurement after cardiac operations. *J Thorac Cardiovasc Surg.* 1987;94(2):286–90.
34. Urzua J. Aortic-to-radial arterial pressure gradient after bypass [letter; comment]. *Anesthesiology.* 1990;73(1):191.
35. Dittrich HC, McCann HA, Wilson WC. Identification of interatrial communication in patients with elevated right atrial pressure using surface and transesophageal contrast echocardiography. *J Am Coll Cardiol.* 1993;21 (Suppl):135A.
36. Schuhmann MU, Suhr DF, v Gosseln HH, Brauer A, Jantzen JP, Samii M. Local brain surface temperature compared to temperatures measured at standard extracranial monitoring sites during posterior fossa surgery. *J Neurosurg Anesthesiol.* 1999;11(2):90–5.
37. Riess FC, Lower C, Seelig C, et al. Recombinant hirudin as a new anticoagulant during cardiac operations instead of heparin: successful for aortic valve replacement in man. *J Thorac Cardiovasc Surg.* 1995;110(1):265–7.
38. Potsch B, Madlener K, Seelig C, Riess CF, Greinacher A, Muller-Berghaus G. Monitoring of r-hirudin anticoagulation during cardiopulmonary bypass—assessment of the whole blood ecarin clotting time. *Thromb Haemost.* 1997;77(5):920–5.
39. von Segesser LK, Mueller X, Marty B, Horisberger J, Corno A. Alternatives to unfractionated heparin for anticoagulation in cardiopulmonary bypass. *Perfusion.* 2001;16(5):411–6.
40. Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia and cardiac surgery. *Ann Thorac Surg.* 2003;76(2):638–48.
41. Harris B, Manecke Jr GR, Niemann J, Madani M, Jamieson S. Deep hypothermia and the vascular response to thiopental. *J Cardiothorac Vasc Anesth.* 2006;20(5):678–83.
42. van der Linden J, Ekroth R, Lincoln C, Pugsley W, Scallan M, Tyden H. Is cerebral blood flow/metabolic mismatch during rewarming a risk factor after profound hypothermic procedures in small children? *Eur J Cardiothorac Surg.* 1989;3(3):209–15.
43. Yoshitani K, Kawaguchi M, Sugiyama N, et al. The association of high jugular bulb venous oxygen saturation with cognitive decline after hypothermic cardiopulmonary bypass. *Anesth Analg.* 2001;92(6):1370–6.
44. Henson LC, Calalang C, Temp JA, Ward DS. Accuracy of a cerebral oximeter in healthy volunteers under conditions of isocapnic hypoxia. *Anesthesiology.* 1998;88(1):58–65.
45. Daubeney PE, Pilkington SN, Janke E, Charlton GA, Smith DC, Webber SA. Cerebral oxygenation measured by near-infrared spectroscopy: comparison with jugular bulb oximetry. *Ann Thorac Surg.* 1996;61(3):930–4.
46. Chen CS, Leu BK, Liu K. Detection of cerebral desaturation during cardiopulmonary bypass by cerebral oximetry. *Acta Anaesthesiol Sin.* 1996;34(4):173–8.
47. Manecke Jr GR, Kotzur A, Atkins G, et al. Massive pulmonary hemorrhage after pulmonary thromboendarterectomy. *Anesth Analg.* 2004;99(3):672–5.
48. Dittrich HC, Nicod PH, Chow LC, Chappuis FP, Moser KM, Peterson KL. Early changes of right heart geometry after pulmonary thromboendarterectomy. *J Am Coll Cardiol.* 1988;11(5):937–43.
49. Dittrich HC, Chow LC, Nicod PH. Early improvement in left ventricular diastolic function after relief of chronic right ventricular pressure overload. *Circulation.* 1989;80(4):823–30.
50. Jamieson SW, Kapelanski DP. Pulmonary endarterectomy. *Curr Probl Surg.* 2000;37(3):165–252.
51. Levinson RM, Shure D, Moser KM. Reperfusion pulmonary edema after pulmonary artery thromboendarterectomy. *Am Rev Respir Dis.* 1986;134(6):1241–5.
52. Thistlethwaite PA, Madani MM, Kemp AD, Hartley M, Auger WR, Jamieson SW. Venovenous extracorporeal life support after

- pulmonary endarterectomy: indications, techniques, and outcomes. *Ann Thorac Surg.* 2006;82(6):2139–45.
53. Berman M, Tsui S, Vuylsteke A, et al. Successful extracorporeal membrane oxygenation support after pulmonary thromboendarterectomy. *Ann Thorac Surg.* 2008;86(4):1261–7.
54. Olman MA, Auger WR, Fedullo PF, Moser KM. Pulmonary vascular steal in chronic thromboembolic pulmonary hypertension. *Chest.* 1990;98(6):1430–4.
55. Moser KM, Metersky ML, Auger WR, Fedullo PF. Resolution of vascular steal after pulmonary thromboendarterectomy. *Chest.* 1993;104(5):1441–4.
56. Thistlethwaite PA, Kaneko K, Madani MM, Jamieson SW. Technique and outcomes of pulmonary endarterectomy surgery. *Ann Thorac Cardiovasc Surg.* 2008;14(5):274–82.
57. Edwards EB, Roberts JP, McBride MA, Schulak JA, Hunsicker LG. The effect of the volume of procedures at transplantation centers on mortality after liver transplantation. *N Engl J Med.* 1999;341(27):2049–53.
58. Menzel T, Kramm T, Mohr-Kahaly S, Mayer E, Oelert H, Meyer J. Assessment of cardiac performance using Tei indices in patients undergoing pulmonary thromboendarterectomy. *Ann Thorac Surg.* 2002;73(3):762–6.
59. Thistlethwaite PA, Madani M, Jamieson SW. Outcomes of pulmonary endarterectomy surgery. *Semin Thorac Cardiovasc Surg Fall.* 2006;18(3):257–64.
60. Corsico AG, D'Armini AM, Cerveri I, et al. Long-term outcome after pulmonary endarterectomy. *Am J Respir Crit Care Med.* 2008;178(4):419–24.

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Key Points

- Pediatric patients present in varying stages of development, from the premature neonate to full-grown teenager. Appreciation of the unique physiologic states associated with the different stages of development will direct anesthetic management.
- Preoperative evaluation of the small child should include the neonatal history as this may indicate comorbid pulmonary and cardiac disease and linked syndromes which must be investigated.
- Lung isolation is not always necessary in pediatric thoracic surgery. Appropriate lung isolation techniques will depend on the age and size of the patient as there is no single technique that is suitable for all pediatric patients.
- Physiologic manifestation of one-lung ventilation may be more pronounced in children than in adults. The compliant rib cage, compressible lung parenchyma, reduced FRC under anesthesia and higher oxygen consumption in the child contribute to aggravate hypoxemia during lung isolation.
- Adult thoracic surgery is often related to tumor excision whereas pediatric thoracic disease encompasses a greater variety of pathology. Each specific disease state has its own particular anesthetic considerations and management strategy.
- Pain management in the pediatric population has evolved to include a greater use of regional and neuraxial techniques, even in the smallest of infants.

- Postoperative disposition will depend on the type and length of surgery, extent of resection or manipulation, and nature of the underlying condition. Many pediatric patients will require postoperative ventilation or close cardiorespiratory monitoring following the procedure.

Introduction

Pediatric and neonatal thoracic anesthesia begins with an understanding of the physiologic and anatomic differences that occur in this patient population. Pediatric patients will present in varying sizes and weights from less than 1 kg to greater than 100 kg, and in varying stages of development from the extremely premature to the older teenage child. It is therefore the requirement of the pediatric anesthesiologist to understand the physiologic differences associated with these extremes and how they influence anesthetic management.

The determinants of these physiologic restraints and the practicality of securing ventilation and oxygenation will often dictate both the anesthetic management and the surgical approach. Unlike the adult population where one-lung isolation can almost universally be applied, in much of the neonatal population this can be at best a harrowing challenge or even an impossibility. As well, securing invasive monitors such as arterial or central venous lines may be problematic in the pediatric population. This means that the pediatric anesthesiologist must appreciate the compromise that arises due to the nature of the patient and procedure, and yet be flexible

and knowledgeable enough to safely carry out the anesthetic management. Postoperative pain management and monitored postoperative disposition may differ significantly from that of the adult population and depend largely on the disease process, surgical intervention, and the physiologic maturity of the patient. Thoracoscopic procedures continue to be applied to smaller and younger patients with their own set of unique challenges and hazards.

The purpose of this chapter is to provide the anesthesiologist with the basic physiologic and anatomic characteristics associated with this patient population and how these differences are practically managed. A general discussion on the cardiopulmonary development of the pediatric patient will be presented, however specialty texts should be sought for in-depth coverage of this topic. Case presentation and examples will be used where possible to provide the reader with a practical approach to common pediatric thoracic procedures. The understanding and practice of these techniques should then enable the pediatric anesthesiologist to apply this knowledge to more complicated and challenging cases.

Pediatric Growth and Development

Normal embryonic development begins at the time of conception and continues throughout the first 8 weeks of life. During this period of time, fetal cells will divide and begin the process of organogenesis. By the fourth week of embryonic development, the primitive heart and lungs appear. At this point neuroulation also begins, a process that will see the eventual creation of the brain and spinal cord.

From this early lung, the trachea and bronchial tree will emerge, and by the eighth week of life the segmental bronchi and diaphragm are complete. In the following months, the airways will canalize and surfactant will be produced. Although lung maturation will continue post delivery, it is generally accepted that by the 27th week of gestation fetal lung maturity is sufficient to sustain ex-uterine life.

Similarly the heart tube which began to beat at approximately day 22 will undergo a series of foldings and septate formation such that the four-chambered heart will be complete at the eighth week of gestation. Shortly thereafter, the valves separating these chambers will also form. Once the process of organogenesis is complete, the remainder of fetal development is devoted to an increase in cell numbers and the maturation of these organs. Intestinal rotation will proceed as well as a significant increase in overall size and weight. Interruption of this normal developmental pathway can have significant impact on the fetus. Teratogens acting at the time of organogenesis can impact organ formation. Abnormal morphogenesis may lead to cleft palate and congenital diaphragmatic hernia (CDH) among others. Chromosomal abnormalities, those that are not lethal, may have a cluster of symptoms that when grouped together form the basis of pediatric syndromes. As well the problems associated with premature infants (born

<37 week GA) are almost entirely due to the immature nature of the fetal organ systems.

Lung and airway maturation continues until approximately the eighth year of life, during which time the number and size of alveoli steadily increase. Transition from intrauterine to the extra uterine environment will see the replacement of the previously fluid filled alveoli with air as the first breaths are taken. As well the alveolar oxygen partial pressure will increase from that of intrauterine life and the oxygen-Hb dissociation curve will begin to transition rightward.

The anatomic changes that the airway undergoes from that of the neonate to infant and onwards to adulthood have been well described. The glottic opening is typically located at the level of the third cervical vertebra as opposed to C4-5 in adults. In addition, the tongue is relatively large and the epiglottis is long and floppy in infants up to 1 year in age. As a result the entire tongue of the neonate and infant is located in the oral cavity, whereas only the anterior two thirds of the tongue in older children and adults occupies the oral cavity. This accounts for the propensity to upper airway obstruction in neonates and infants who are sedated, have decreased level of consciousness, or during anesthetic induction. Until 7 or 8 years of age the tracheal diameter at the level of the cricoid cartilage is narrower than that at the vocal cords, resulting in a conical larynx. A tracheal tube that passes through the vocal cords may not necessarily then pass through the cricoid ring. A relatively large head, short neck and trachea mean that tracheal intubation, although not typically difficult, requires a subtly different technique than that used in the adult patient.

As the lungs fill with air during the first moments of extra uterine life, pulmonary vascular resistance (PVR) will fall and cause a dramatic increase in pulmonary blood flow. As PaO_2 rises the ductus arteriosus will constrict and usually fully closes by the end of the first week of life. Left-sided cardiac pressures will rise and close the foramen ovale. The myocardium of the neonate is relatively noncompliant and cannot adjust contractility in response to changes in filling pressures. The cardiac output in the neonate is thus dependent on HR and the normal heart rate is typically between 100 and 150 bpm.

Relative body composition changes also occur during the first year of life. The highest percent body fat is at 1 year of age (approximately 30%) and typically decreases throughout adult life. Total body water (as a percentage of body weight) is highest at birth (75%) and drops to adult (60%) levels by 1 year of age. The estimated blood volume (as a percent of body weight) also decreases. Term infants typically have an estimated blood volume of 95 mL/kg, whereas by 1 year of age it has decreased to 65 mL/kg. In addition to this the fluid, electrolyte composition, energy requirements, hematologic system, and vital signs all change significantly throughout the various stages of growth. The pediatric anesthesiologist's understanding of these changes will necessarily guide the management of the patient as drug dosages, ventilation parameters, and equipment must be adjusted for the age and maturation of the patient.

Special Considerations

Prematurity

Premature infants have several unique features that will briefly be addressed here. In-depth coverage of this topic can be found in any neonatal or pediatric specific anesthesia text.

Fetal surfactant is produced by type II pneumocytes at approximately the 22nd week of gestation. Half of this production is usually complete by the 28th week, with the remainder by the 37th week. Steroid administration to the mother can speed up this process. Deficiency in surfactant production may result in respiratory distress syndrome (RDS) [1]. The constellation of tachypnea, indrawing, and oxygen desaturation results from collapse of alveoli caused by insufficient surfactant levels. This leads to decreased lung compliance, higher opening pressures, decreased FRC, and increased work of breathing. Arterial blood gas analysis will often reveal hypoxemia, hypercarbia, and acidosis.

The early management of RDS consists of oxygenation and assisted ventilation in the form of noninvasive CPAP/BIPAP [2–4]. Exposure to high oxygen concentrations may lead to retinopathy of prematurity (ROP) and other complications in these patients, although the role of anesthetic agents in causing ROP remains undefined. Balancing the need to avoid tissue hypoxemia and avoiding the toxic effects of oxygen can be challenging. Prudence would seem to suggest that using the lowest possible FiO_2 to maintain adequate tissue oxygenation is advisable. Oxygen therapy is often adjusted to achieve an oxygen saturation of 90–93%, however if there is evidence of hypoxia-induced hemodynamic instability or other end-organ failure oxygen therapy should not be sacrificed in order to prevent ROP. Continued oxygen desaturation (below 90%) or persistent acidosis may require endotracheal intubation and mechanical ventilation be instituted. The goal of ventilation is to minimize baro- and volu-trauma while maintaining oxygen saturation between 90 and 93%. To this end, relative hypercapnia (PaCO_2 45–60 mmHg) is often permitted. Much like the management of ARDS, the FiO_2 and PEEP ratio should be carefully adjusted to minimize both while achieving the above stated goals.

Exogenous surfactant can also be administered to these infants both at the time of birth and at regular intervals thereafter [5, 6]. Surfactant acts to decrease alveolar surface tension and has been shown to decrease RDS-related morbidity and mortality [1, 7]. The long-term sequela from RDS is typically bronchopulmonary dysplasia (BPD). These children may continue to have respiratory difficulty secondary to decreased lung compliance and increased airway resistance with increased dead space.

Pulmonary Hypertension

Pulmonary hypertension is classically defined as mean pulmonary arterial pressure (PAP) >25 mmHg at rest or >30 mmHg with activity [8]. In neonates, echocardiographic evidence of

TABLE 39.1. Causes of persistent pulmonary hypertension in the newborn.

Acute pulmonary vasoconstriction due to perinatal events

- Meconium aspiration
- Respiratory distress syndrome
- Pneumonia
- Hypoventilation/asphyxia
- Hypothermia
- Hypoglycemia
- Sepsis

Idiopathic

- Maternal NSAID or SSRI use
- Pulmonary vascular hypoplasia
 - Congenital diaphragmatic hernia
 - Oligohydramnios
 - Congenital cystic adenomatoid malformation (CCAM)

Pulmonary sequestration

- Cardiac lesions
 - Pulmonary atresia with intact ventricular septum
 - Transposition of the great arteries (TGA)
 - Total anomalous pulmonary venous drainage (TAPVD)
 - Tricuspid atresia

PVR greater than the half the systemic vascular resistance is commonly considered as evidence of pulmonary hypertension [9]. This state arises when PVR fails to decrease after the transition to extra-uterine life occurs. Severely elevated pulmonary pressures will cause a decrease in blood flow through the lungs and encourage right-to-left shunting, resulting in cyanosis and hypoxemia. The causes of persistent pulmonary hypertension in the newborn are described in Table 39.1.

Management of pulmonary hypertension involves treating the underlying cause and reducing pulmonary vascular tone. To this end supplemental oxygen administration is employed as well as control of ventilation to avoid hypercapnia and acidosis. Pharmacologic pulmonary vasodilators such as intravenous prostacyclin, phosphodiesterase III inhibitors (e.g., Milrinone), and/or inhaled nitric oxide may be administered if necessary [10]. Sildenafil has shown promise and is increasingly being used to treat responsive pulmonary hypertension in this patient population [11, 12]. Individual or combination therapies have been used in neonatal and infant populations with some success [13–15]. Nitric oxide offers the theoretical advantage of improving V/Q matching by preferentially increasing blood flow to ventilated alveoli. Alternatively, extracorporeal membrane oxygenation (ECMO) has been utilized to temporize pulmonary hypertension or as a bridge to lung transplantation [9, 16, 17].

Cardiac Disease

Patent ductus arteriosus (PDA) is a common finding in the premature infant. Blood flow through the PDA is typically left to right, although this can reverse if pulmonary hypertension exists. Preoperative echocardiography should be performed to evaluate this. Depending on the reason for prematurity, these infants may also have other forms of congenital heart

disease (CHD) that should be evaluated prior to undergoing any anesthetic. Although pharmacologic or surgical closure of the PDA is often indicated, if other cyanotic CHD exists the closure of the PDA is delayed until the lesion is repaired or palliated via another form of surgical shunt. The anesthetic management of thoracic procedures in patients with unrepaired or palliated shunts is particularly challenging. Increased positive-pressure ventilation and compromised oxygenation may lead to worsening of right-to-left shunts.

Immature organ function and depleted metabolic reserves predispose the premature infant to several other age-related disorders. Lack of glycogen stores in the premature neonatal liver places these patients at risk for hypoglycemia. The implications of untreated hypoglycemia can be quite severe and include seizures and developmental delay. The normal stress response of surgery is to increase plasma glucose levels secondary to catecholamine and cortisol production. This may not occur, however, in the very sick child. Five or ten percent dextrose solution should be used as maintenance fluid in the pediatric population, although at what age this practice should cease is not clear [18]. To avoid hyperglycemia a balanced salt solution should be used for fluid bolus administration [19].

Apnea of prematurity is common and its incidence is inversely proportional to the gestational age and weight of the child. Apnea (airflow cessation lasting more than 15 s) may be accompanied by bradycardia and hypoxia. The presumptive mechanism is due to immature neuronal control at the level of the brainstem and peripheral chemoreceptors [20]. An obstructive component to the apnea is often present as well. Other risk factors include a hemoglobin <100 or Hct<30. Management may include minimizing narcotic use, stimulation and airway support, and pharmacologic (e.g., caffeine). Postoperative observation and monitoring for apnea is mandatory in premature and ex-premature infants less than 50–60 weeks postconceptual age.

Preoperative Evaluation

As in adults the preoperative evaluation of the pediatric patient focuses on the history, physical exam, and laboratory investigations, although an age-appropriate evaluation is necessary. The pediatric practitioner must be aware that certain congenital anomalies do not occur in isolation. For example, tracheoesophageal fistula may be associated with other significant anomalies as part of the VACTERL syndrome (vertebral, anal, cardiac, TE fistula, renal, radial, and limb anomalies). The presence and severity of the associated anomalies should be identified as they may affect anesthetic management.

The evaluation of the neonate or infant typically begins with a history of the pregnancy, labor, and delivery. APGAR scores and resuscitation efforts at delivery are important as they may provide diagnostic clues. For example, prolonged tracheal intubation early in life may predict the presence of subglottic stenosis. RSD leading to BPD may affect children many years after their NICU discharge. Both these examples

may lead the anesthesiologist to modify his approach to airway management or ventilation strategy.

As this may be the first anesthetic the child is to receive, the biological parents must be questioned with regard to prior familial anesthetic complications. Malignant hyperthermia and pseudocholinesterase deficiency (among others) have a genetic transmission and may present with the first anesthetic. If a prior anesthetic record is available it should be reviewed. As in adults particular attention should be focused on the ease of bag mask ventilation and intubation. In the pediatric population, one must also look for evidence of difficulty with intravenous access and the disposition of the child prior to induction. Endotracheal tube (ETT) size and the presence of a leak around the tracheal tube should also be noted.

Functional capacity should be assessed keeping in mind the patient's age. An infant's inability to take full feeds, sweating, and/or cyanosis during feeds may be an indicator of heart failure. In toddlers and older children, activity level or ability to run or play is a better measure of cardiothoracic functional capacity. A helpful indicator is whether the child is able to keep up with his peers when at play. A child who takes more frequent naps or must stop and sit while his peers continue to play is a clear indication of decreased functional capacity. Height- and weight-based growth analysis will also provide evidence of failure to thrive which can be caused by or exacerbate a decreased functional capacity.

The physical exam can be challenging in the pediatric patient. Noncompliance and occasionally combativeness will prevent thorough examination. Most adult markers for difficult bag mask ventilation and intubation are not appropriate for infants and children. Assessing Mallampati score in a newborn may be impossible and futile. In its place many pediatric anesthesiologists assess the craniofacial silhouette or profile, focusing on evidence of retro- or micrognathia. A gloved finger can also be used to feel for the presence of a high arched and/or cleft palate, which may be associated with difficult laryngoscopy.

Respiratory compromise or distress will manifest not only as tachypnea, but perhaps also as indrawing, nasal flaring, grunting, accessory muscle use, or paradoxical breathing. All are easily identifiable in children. Peripheral cyanosis and evidence of decreased perfusion should be sought. Assessment of intravascular volume status in the pediatric patient may be challenging. Orthostatic vital signs are generally not done in neonates and the JVP cannot be easily seen. Skin turgor, capillary refill, fontanelle fullness, level of consciousness, and urine output, however, are easily assessed, as is total fluid intake. A newborn that consistently is gaining weight is very unlikely to be hypovolemic.

Vital signs change with age and should therefore be compared to the statistical norms for the patients' cohort. Blood pressure measurements in an irritable or uncooperative child can be unreliable or impossible to attain. Auscultation for normal heart sounds and murmurs of concern is important to document. Evidence of heart failure, pulmonary edema, and wheezing on respiratory exam should also raise concerns.

Laboratory investigations in the pediatric population should be based on the presenting illness and the surgery proposed. Often children that are booked for thoracic procedures will have at minimum a CXR that can be evaluated for pulmonary pathology, edema, and evidence of scoliosis and engorgement of the vascular structures. If available the computed tomography (CT) scan or MRI should also be viewed. This will prove a valuable aide in determining the feasibility of lung isolation and the extent of the pathology. Particular attention should be noted if the disease is in communication with the bronchi (e.g., congenital cystic adenomatoid malformation, CCAM) as this will potentially alter the ventilation strategy. Anterior mediastinal masses may compress the great vessels, the trachea, or the heart itself. Evidence of cardiovascular compromise, whether on history or physical exam, warrants further investigation with transthoracic echocardiography. Often an understanding of the disease pathophysiology and associated cardiac anomalies will warrant this investigation. An ECG can be very helpful in these circumstances.

Since most thoracic procedures have the potential for blood loss as a minimum a CBC should be obtained preoperatively. This test may also indicate the degree of hypoxia if the hematocrit is significantly elevated. Often electrolytes and renal function indicators will be ordered. In an otherwise healthy child, no blood work may be needed. Baseline arterial blood gases may be useful but may not be practical in the frightened young child. Capillary or venous gases are more easily obtained in pediatrics and provide almost as much useful information as arterial gases. Unlike the adult patient that presents for thoracic surgery, it is often impossible to obtain reliable pulmonary function tests or spirometry. This, however, should not be an impediment to proceeding with the planned surgery. Any further testing should be based on those areas of concern elucidated during the preoperative evaluation.

Lastly, the preoperative evaluation should be used to explain to the child and/or parents the anesthetic plan and the eventual disposition of the patient. Risks and complications should be addressed and assent or consent obtained. Decisions regarding preoperative sedation and parental presence at induction can also be made at this time. The postoperative pain management strategy should be outlined and questions or concerns addressed.

Strategies for Lung Isolation

The indications for lung isolation in children include prevention of contamination by blood or pus, treatment of a large bronchopleural fistula or severe unilateral bronchiectasis, as well as facilitating surgical exposure during thoracic procedures. Although thoracoscopic procedures may be performed without lung isolation in very small infants (the induced pneumothorax is often enough to compress the lung tissue and provide surgical exposure, see Fig. 39.1), one must be prepared to isolate the lungs in the event surgical exposure is inadequate. The techniques and approach to lung isolation in

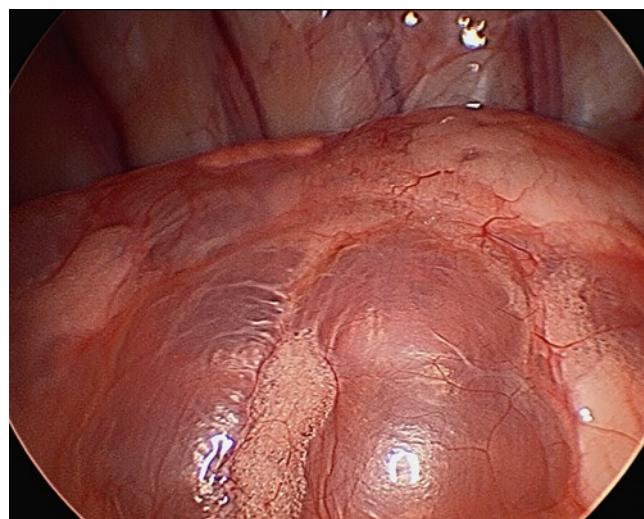


FIG. 39.1. Thoracoscopic view of a 6-month-old infant's right hemithorax in whom adequate surgical lung exposure was achieved with the induced capnothorax and without the need for lung isolation. The right lower lobe almost entirely consists of congenital cystic adenomatoid malformation (CCAM).

the pediatric population may differ from that of adults since infant and small child-sized bronchial tubes are not available. Despite this, the basic principles of lung isolation in the child are similar to those for the adult. There are three fundamental techniques of lung isolation: single lumen endobronchial intubation, bronchial blockers, and double lumen bronchial tubes [21].

Historically, the use of single-lumen tubes for selective endobronchial intubation was the only method to isolate the lungs in small children. Although it is now rarely the preferred method of lung isolation, it has the advantage of being readily available, requiring little technical expertise and can be performed on any patient, regardless of size. Right mainstem bronchus intubation is easily accomplished and has been performed (inadvertently or otherwise) by virtually every anesthesiologist. Left mainstem bronchus intubation, if done blindly, simply requires the ETT be rotated 180° with the patient's head turned to the right. This maneuver turns the bevel of the tracheal tube to favor left mainstem bronchus intubation with advancement. Alternatively, flexible fiberoptic bronchoscopy can be used to place the tracheal tube in the appropriate mainstem bronchus under indirect vision. Regardless of which technique is used fiberoptic verification of proper tube placement is recommended [22, 23].

Other advantages of this technique include very rapid isolation that can be applied in emergency situations such as pulmonary hemorrhage. Limited technical experience is required and specialized equipment is not necessary. Because single-lumen tubes are available in a wide variety of sizes there is no patient that cannot be managed by this method. Note, however, that since airway diameter narrows further down the trachea and bronchi, one should consider placing a slightly smaller ETT than otherwise indicated.

Disadvantages of this technique are numerous. Firstly, conversion to temporary two-lung ventilation (i.e., to reexpand the nondependent lung) may be cumbersome. This requires withdrawing the secured ETT from the bronchus to the trachea. Reisolating the lung with the patient in lateral decubitus position and under surgical drapes can be problematic. As well, an incomplete seal at the bronchus will allow gases to escape and inflate the nondependent lung. Leak gas will also contaminate the room; however, more importantly debris, blood, and secretions from the operative side may soil the poorly isolated lung. If intubating the right mainstem bronchus, obstruction of the right upper lobe is possible, especially if a cuffed ETT is used. Finally, if hypoxemia arises it is impossible to apply CPAP to the nondependent lung. If adjusting PEEP to the dependent lung does not improve the hypoxemia repositioning the ETT above the carina and reverting to two-lung ventilation will be the only solution.

Bronchial blockers play an important role in pediatric lung isolation, particularly in patients 3 months to 9 years of age. There are currently three main devices available: Fogarty arterial embolectomy catheters (Edwards Lifesciences, Irvine, CA, USA), Univent® tube (Vitaid, Lewiston, NY, USA), and the Arndt endobronchial blocker (Cook® Critical Care, Bloomingdon, IN, USA). The use of the Fogarty catheter for lung isolation is well described and has been used for all types of thoracic procedures [24–27]. The catheter can be placed either alongside the standard ETT or within it. If it is to be placed outside the ETT the catheter is advanced under direct laryngoscopy through the vocal cords. The blocker catheter tip (which if larger than 3F can be slightly flexed, see Fig. 39.2) is then rotated 90° toward the desired lung and advanced into the mainstem bronchus. The ETT is then placed in the trachea. With fiberoptic visualization the position of the catheter can be verified prior to inflation of the balloon tip. The entire apparatus is then secured to the patient.

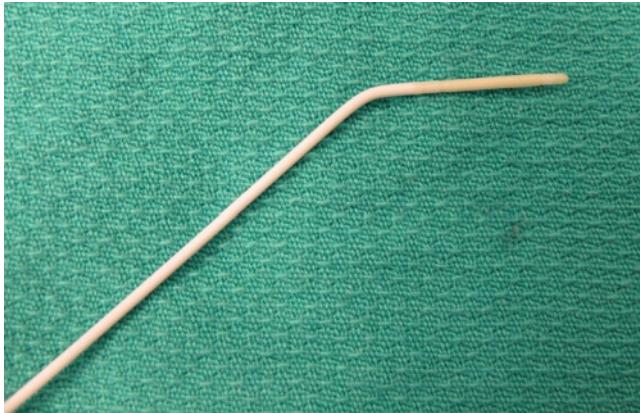


FIG. 39.2. Tip of a size 4F Fogarty embolectomy catheter (Edwards Lifesciences, Irvine, CA, USA) which has been shaped to facilitate maneuverability and insertion into a mainstem bronchus. All Fogarty embolectomy catheters except the size 2F and 3F contain a removable guide wire that can be used to shape the tip in this fashion.

If the Fogarty catheter is to be placed within the lumen of the ETT, the method of placement is as follows. As described earlier for selective endobronchial intubation, the ETT is advanced into the desired bronchus. The 15-mm adapter is removed from the tracheal tube and the Fogarty catheter is placed through the lumen of the ETT into the bronchus. The ETT is withdrawn to a position above the carina while maintaining the endobronchial position of the catheter. Again verification and inflation of the Fogarty should be performed under flexible fiberoptic visualization. The ETT adapter will then have to be securely fastened such that the Fogarty is trapped between the adapter and ETT itself (see Fig. 39.3). A disadvantage of placing the Fogarty within the lumen of the ETT is that it may significantly decrease the internal diameter. This can interfere with ventilation if using a very small ETT but more commonly it will make passage of the fiberoptic scope difficult. The fit of all scopes and airway devices must be prepared and tested prior to anesthetic induction.

The main advantage of the Fogarty catheter is that it can be used in very small infants as well as older children. Table 39.2 outlines the various embolectomy catheter sizes as well as the corresponding appropriate tracheal tube sizes used in pediatric practice. In general, the smaller the patient the more challenging proper catheter placement becomes. Deflation of the balloon tip will enable easy and rapid reexpansion of the operative lung without requiring manipulation of the ETT.

A drawback to the Fogarty catheter is that the balloon is a low-volume, high pressure device. For this reason, balloon inflation should be done under direct visualization and only the minimum of pressure be applied to provide bronchial sealing.

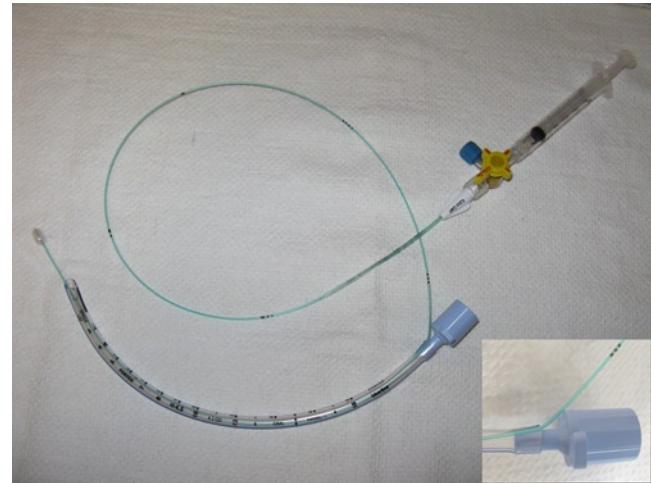


FIG. 39.3. Embolectomy catheter and tracheal tube assembly used for lung isolation in the small child. A size 3F Fogarty embolectomy catheter (Edwards Lifesciences, Irvine, CA, USA) inserted through a 4.5-mm ID tracheal tube (Sheridan) and placed in a mainstem bronchus. The embolectomy catheter is secured in place and sealed between the tracheal tube inner lumen and the 15-mm adapter (inset). Alternatively, the embolectomy catheter may be placed outside the tracheal tube in the mainstem bronchus.

TABLE 39.2. Bronchial blocker sizes used for lung isolation in children.

Age	ETT size (ID, mm)	Bronchial blocker size (F) ^a	Max balloon gas capacity (cc)	Inflated balloon diameter (mm)
<2 months	3.0–3.5	3	0.6	5
2–6 months	3.5–4.0	4	1.7	9
6 months – 1 year	4.0	4	1.7	9
1–2 years	4.0–4.5	5	3.0	11
2–4 years	4.5–5.0	5	3.0	11
4–6 years	5.0–5.5	5	3.0	11
6–8 years	5.0–5.5	6	4.5	13
8–10 years	5.5–6.0	6	4.5	13

ETT endotracheal tube; ID internal diameter

^aFogarty arterial embolectomy catheters (Edwards Lifesciences, Irvine, CA, USA)

Table 39.2 illustrates the maximum inflation volumes of the various embolectomy catheters. Since migration of the blocker by even a few millimeters can cause the balloon to slip into the lumen of the trachea and obstruct both lungs one must be vigilant and prepared to immediately intervene by deflating the catheter cuff.

The Univent® tube has been designed with a channel that contains a bronchial blocker. Conventional laryngoscopy places the single-lumen tube into the trachea and fiberoptic guidance of the balloon tipped catheter into the operative lung can then be performed. When seated appropriately, the Univent will isolate the lung and allow for easy conversion to conventional two-lung ventilation by simply deflating the bronchial cuff.

Pediatric sizes are available as small as 3.5 mm internal diameter. However, this device has an 8-mm external diameter and as such should not be used in patients less than 6 years old. In these smaller tube sizes, the bronchial blocker and its channel will also encroach into the lumen of the ETT and proportionally increase the airflow resistance as well as necessitate the use of a smaller fiberoptic scope. Univent® tubes below 6.5 mm ID do not have a central lumen in the bronchial blockers. Therefore, oxygen and CPAP cannot be applied with the smaller Univent® tubes [28–30].

The Arndt endobronchial blocker is a more recent addition to the armamentarium available to the pediatric anesthesiologist [31–33]. It consists of a conventional blocker with balloon tip and four-way adapter. The balloon is designed as a high-volume low-pressure system. Pediatric sizes include a 5F and 7F size blocker which can be used in a 4.5- and 6.5-mm ID tracheal tube, respectively (Table 39.3). Preparation and use of the Arndt endobronchial blocker is identical to that for adults (see Chap. 16). As proportionally more of the ETT lumen is occupied by the blocker airway resistance and pressures will increase.

A unique challenge of using the pediatric sized Arndt blocker is adequate ventilation while the blocker and FOB both

TABLE 39.3. Pediatric Arndt endobronchial blocker sizes^a.

Blocker	ETT size (ID, mm)	FOB size (OD, mm)	Balloon inflation volume (cc)
5.0	≥4.5	≤2.8	0.5–2.0
7.0	≥6.5	≤3.5	2.0–6.0

ETT endotracheal tube; ID internal diameter; OD outer diameter

^aCook® Critical Care, Bloomington, IN, USA

occupy the lumen of the ETT. The smallest sized FOB must be used that allows placement of the endobronchial blocker. If such a small (i.e., 2.2 mm OD) fiberoptic bronchoscope is not available, the blocker can be positioned outside the ETT much like an embolectomy catheter. The tip of the FOB is passed through the nylon loop of the blocker and the assembly is inserted in the operative bronchus. The FOB is then removed and the tracheal tube placed using direct laryngoscopy. Alternatively, if the patient remains adequately oxygenated and ventilated with the FOB-blocker apparatus in the operative bronchus, the FOB may be withdrawn to a position above the blocker and inflation of the blocker cuff can be observed prior to removing the FOB. Once in position the nylon guide can be removed from the bronchial blocker (it cannot later be reinserted) and the central channel can be used for suctioning, providing supplemental oxygen, and CPAP. Fuji Systems (Tokyo, Japan) has recently released a 5F pediatric size of its independent bronchial blocker, the Uni-Blocker®.

The double-lumen endobronchial tube (DLT, Bronchopart®; Rüsch Inc, Duluth, GA, USA) differs significantly from the above designs in that selective intubation of either mainstem bronchus can be achieved with a second lumen located within the trachea. In this way, ventilation can be applied through either lumen individually or collectively. Unfortunately, pediatric sizes are limited due to the necessarily larger outer diameter of such a design. The 26-F is currently the smallest available size and has an outer diameter of 9.3 mm, equivalent to a 6.5-mm ID ETT [34]. It is suitable for children approximately 8–10 years of age or approximately 30 kg in weight. Below this, one of the aforementioned isolation techniques is more appropriate. Double-lumen tube sizing will depend on the child's height as well as age. In general, a 28F DLT is suitable for a 12-year-old child, a 32F is appropriate for a 14-year old, and a size 35F is suitable for a 16-year old.

The DLT is straightforward in its application. Conventional laryngoscopy places the device into the trachea where it can be advanced into position by rotation to the appropriate side in a manner identical to that for adult patients. Fiberoptic bronchoscopy is recommended to ensure proper positioning [35]. Most often a left-sided DLT is used as it is easier to insert and eliminates the risk of right upper lobe obstruction. Correct positioning will mean the bronchial lumen is within the appropriate mainstem bronchus and the tracheal lumen above the carina. Inflation of the bronchial cuff can be observed with the FOB placed within the tracheal lumen. Once inflated the specialized circuit adapter can be manipulated such that

ventilation to that lumen is obstructed while egress of gases from the lung is permitted.

Advantages of the DLT include easy access to either lung for suctioning or ventilation, application of supplemental oxygen, and CPAP. Conversion to two-lung ventilation is rapid and simple. Disadvantages of the DLT are mainly due to its awkward size and shape. Iatrogenic injury has been reported and placement in patients with a difficult airway may be particularly challenging [36, 37]. The DLT should be replaced with a conventional ETT if postoperative ventilation is required.

Anesthetic Management of Specific Procedures and Diseases

Bronchoscopy

Evaluation of the airway by bronchoscopy, either rigid or flexible, has both diagnostic and therapeutic indications [38]. It is one of the few pediatric thoracic procedures that can be performed outside of the operating room under sedation or general anesthesia. In fact, depending on the age of the patient and indication for bronchoscopy the anesthesiologist may not be involved at all, as some pediatric pulmonologists will provide airway topicalization and intravenous sedation in an ambulatory setting. This approach should be reserved for older, cooperative children who do not have severe respiratory compromise. Those patients that do require operative bronchoscopy must be evaluated with particular focus on the reason for bronchoscopy and the level of respiratory derangement. The type of procedure will often determine the means by which the airway is maintained, the type of anesthetic to be given, and whether paralysis is warranted. Rigid bronchoscopy for foreign body removal will require that a general anesthetic be given. Diagnostic evaluation of the trachea and bronchi for other etiologies can generally be performed via flexible bronchoscopy. Communication between the bronchoscopist and anesthesiologist is essential in any such shared airway case. An appropriately sized ETT or supralaryngeal airway should be selected for the specific fiberoptic bronchoscope in order to ensure ventilation can be maintained during bronchoscopy.

Older children who are able to understand and cooperate with the anesthesiologist and bronchoscopist can be successfully managed with airway topicalization and intravenous sedation. This can include an infusion of one or a combination of propofol, remifentanil, or ketamine, with or without midazolam [39–43]. More recently, an infusion of dexmedetomidine and propofol has been used in this setting [44]. Although ideally this should be carried out in the OR setting, such procedures are now frequently performed outside the operating room to contain costs and increase efficiency. Children tend to need a deeper level of sedation than adults in order to tolerate the bronchoscope and titrating the sedation/anesthesia to achieve acceptable procedural conditions while maintaining

spontaneous respiration can be challenging. Monitoring and preparation for possible conversion to a general anesthetic is essential. A second physician for patient monitoring and airway management should be at hand.

For those patients that are not suitable for sedation and airway topicalization, several options for airway management exist. These include but are not limited to mask ventilation, laryngeal mask, endotracheal intubation, and ventilation through the side port of a rigid bronchoscope [45]. Face mask ventilation has an advantage over the other methods listed as it allows for fiberoptic inspection of the oropharynx and/or nasopharynx and can be managed by one of two methods. The simplest is intermittent bag-mask ventilation or support with bronchoscopy conducted while the mask is temporarily removed from the patient. This requires coordination between the anesthesiologist and bronchoscopist and may involve periods of hypoventilation or apnea. If an inhalation agent is chosen as the means of anesthesia then both awareness and waste gas pollution are a concern as the patient will be exhaling the agent into the room during the procedure. Careful titration of TIVA may therefore be the preferred approach for this option [46]. In addition, the diagnostic value of the procedure may be impaired as the bronchoscopist must enter and exit the airway repeatedly. To overcome these limitations face masks with angled side ports have been developed that allow for continuous application of the mask to the patient and ventilation through the adapter while the bronchoscopist uses an inline diaphragm that minimizes gas leakage (Fig. 39.4).

Although the laryngeal mask does not allow for inspection of the upper airway, it has nevertheless become the most commonly used conduit for diagnostic and therapeutic bronchoscopy in the pediatric patient outside the critical care unit [47]. The availability of smaller sizes and its ease of use make it ideally suited for this procedure. It is better tolerated than a



FIG. 39.4. Pediatric endoscopy mask (VBM Medizintechnik GmbH, Sulz, Germany) designed to allow simultaneous ventilation and endoscopy of the child. The assembly may be used for flexible fiberoptic intubation or airway endoscopy.

tracheal tube and accommodates both spontaneous ventilation and positive pressure ventilation as required. It has been shown in several studies to be well suited for bronchoscopy, even in small infants [48–50]. An angled adapter with an inline diaphragm for the bronchoscope is required. If the LMA has aperture bars, they may need to be removed as they can impair the scope from passing through. In most cases, the bronchoscope will align itself with the glottic opening and not require any further manipulation of the LMA once seated.

Endotracheal intubation provides the most secure, stable, and controlled means of airway management for bronchoscopy. The majority of children in the critical care unit undergoing bronchoscopy will have an ETT in situ and undergo bronchoscopy to assess bronchial patency or pathology, tracheomalacia, and for sputum sampling. Outside the critical care unit, elective tracheal intubation for bronchoscopy may be preferred for infants and small children as well as patients with significant respiratory compromise. A period of postoperative ventilation may also be required for high-risk patients. Disadvantages of bronchoscopy through an ETT include the inability to examine the upper airway as well as bronchoscope size limitations. An appropriately sized scope must be chosen that allows adequate ventilation around itself in the remaining lumen of the ETT.

Rigid bronchoscopy offers the advantage of allowing dynamic examination of the airway from the oropharynx to the subsegmental bronchi. Most pediatric rigid bronchoscopes contain a 15-mm side port that allows for gas insufflation and even positive pressure ventilation. It is the instrument of choice for pediatric foreign body removal. Disadvantages of rigid bronchoscopy include the fact that deep anesthesia is required to tolerate the bronchoscope and, if volatile anesthetic agents are used, room air contamination is a concern. In that case, suction or gas scavenging can be positioned at the base of the bronchoscope to minimize contamination. The practice of many pediatric anesthesiologists is to therefore use a propofol-based TIVA technique with local anesthetic applied to the vocal cords and carina. To this end a low dose (i.e., 0.05 µg/kg/min) remifentanil infusion may be a useful adjunct. Typical goals are to maintain spontaneous ventilation without the use of muscle relaxants. However, positive pressure ventilation can be applied via the side port of the rigid bronchoscope which may be facilitated by muscle relaxation.

Fever is not an uncommon sequela of flexible bronchoscopy and it is not necessary to treat all such patients with antibiotics. Case reports of fever associated with sepsis following bronchoscopy have been reported, however these are generally in immunocompromised patients in whom antibiotic therapy is warranted [51, 52]. Similarly rigid bronchoscopy has been shown to induce transient bacteremia, but again antibiotic treatment is generally unnecessary. Complication rates for bronchoscopy are low. The most common adverse event is transient desaturation, however, laryngospasm and bronchospasm can also occur [53, 54].

Thoracotomy and Video-Assisted Thoracoscopic Surgery (VATS)

Traditionally, all thoracic procedures in children were performed via a thoracotomy or median sternotomy. Mechanical retraction of the ribs and lung tissue would often be applied to provide the required surgical exposure. Because of technological advances and greater surgical experience gained from the adult population, video-assisted thoracoscopic surgery (VATS) is now used more readily in the pediatric population, even at the extremes of age and weight (Fig. 39.5) [55–58]. The reported advantages of VATS in the adult population, including less postoperative pain and shorter length of stay accelerated the use of this technique in children. Although very few outcome studies have been conducted in children, VATS is utilized for an increasing number of conditions including empyema, lung biopsy and resection, mediastinal mass, trauma, pulmonary sequestration, and CCAM (Fig. 39.1) [59]. Even PDA closure is being performed thoracoscopically in very small infants [60]. Trocars for pediatric use are available in 5 and 3 mm diameters (Fig. 39.5).

Whereas thoracotomy does not always require the lungs be isolated in children, VATS is quite challenging without proper lung isolation and collapse of the surgical lung. An exception is in small infants, whose lungs can be collapsed with the induced capnothorax.

Single-lung ventilation in the pediatric population incurs many of the same physiologic derangements as in the adult population (see Chap. 6). Collapse of the nondependent lung preferentially directs ventilation to the dependent (nonsurgical) lung. Hypoxic pulmonary vasoconstriction (HPV) in the nondependent lung increases perfusion to the dependent lung and therefore attempts to correct the shunt. In adults with the



FIG. 39.5. Thoracoscopic trocars inserted in an infant for VATS. Surgical trocars used in children are available in 5 mm (shown) and 3 mm diameters.

diseased lung in a nondependent position, this arrangement may actually improve oxygenation. Unfortunately in infants and neonates, this is often not the case. A compliant rib cage and compressible lung parenchyma allows for mediastinal excursion into the dependent lung thus reducing ventilation of that lung. Poor positioning and increased insufflating pressures will further contribute to this. Decreased hydrostatic pressure gradients between the two hemithoraces translate into relatively little improvement in V/Q matching even when HPV is intact. Moreover, alveolar collapse occurs more readily in infants as FRC approaches residual volume. The higher ratio of oxygen consumption to FRC, as compared to adults, will further exacerbate deoxygenation.

Many of the same complications of VATS occur in the pediatric population as in adults. Trocar misplacement (into the spleen or liver) may cause significant morbidity. High thoracoscopic insufflating pressures will decrease cardiac output and blood pressure by reducing preload and afterload. Patient positioning is even more important in pediatric procedures as an inappropriately located bolster will easily compress the compliant rib cage and reduce lung volumes in the dependent lung. Abdominal compression in the lateral decubitus position, from padding or “bean bags” will force the abdominal contents into the chest. As with any procedure that involves CO_2 insufflation under pressure, CO_2 gas embolism, though rare, must be considered in the event of sudden severe hemodynamic derangement.

As in adults maneuvers to preserve and treat hypoxemia with single-lung ventilation apply equally in the pediatric setting. Initial routine use of 100% oxygen upon lung isolation offers an increased safety margin and decreases HPV of the dependent lung. Once the procedure is underway and hemodynamic stability confirmed, the FiO_2 may be decreased as tolerated. Pressure controlled ventilation may be used provided it delivers volumes in the range of 5–10 mL/kg. To this end mild hypercapnia is permitted, to avoid barotrauma. The application of PEEP to the dependent lung may improve oxygenation, and if kept to <10 mmHg usually has minimal effects on PVR and does not divert blood flow away from the ventilated lung. Application of CPAP to the nondependent lung is not as practically applicable in the small child and often interferes with surgical exposure.

To conclude, the decision to proceed with a thoracotomy vs. VATS procedure must be discussed ahead of time by surgeon and anesthesiologist. A thorough understanding of the risks and benefits must be assessed by both teams and then explained to the parents/patient. A discussion between the anesthesiologist and surgeon must include a time line with respect to how long the VATS technique will be employed. If surgical goals are not met during this time line then conversion to thoracotomy should be considered. Most importantly, emergency management of intraoperative bleeding must be discussed and a plan formulated for emergent conversion to thoracotomy. Pediatric patients, especially small infants and neonates, will very rapidly hemorrhage into the chest cavity.

By the time thoracotomy is performed and surgical control of bleeding is established, significant morbidity may have occurred. Resuscitation, even with rapid/immediate transfusion, is extremely difficult in such cases. A low threshold is recommended for release of capnothorax and possible immediate conversion to thoracotomy if significant hemodynamic instability arises.

Empyema

Collection of fluid or pus in the pleural space will occur in approximately 28% of parapneumonic infections [61]. Conventional treatment has been insertion of a chest tube and drainage with continued antibiotic therapy. More recently, the increasing popularity of VATS has challenged this management stratagem. Retrospective studies comparing length of stay, length of antibiotic treatment, and cost analysis favor VATS to conservative management [62–67]. Avansino et al. [68] conducted a meta-analysis of 67 studies with findings indicating a higher success rate in the primary VATS group (failure rate of 23% in the non-VATS group). Furthermore the rate of complications was found to be similar in both groups, although reintervention and salvage operative rates were higher in the conservative group.

The conversion rate from VATS to open thoracotomy was low (<1.5%) as was the VATS failure rate (unresolving empyema following VATS, 2.8%). Open thoracotomy yielded results similar to that of VATS. It must be noted the studies in this analysis were retrospective. As well, greater than 75% of those treated with primary conservative management did improve without the need for surgery (although duration of treatment was longer). This would indicate that perhaps a step-wise approach to empyema management be utilized. This may include chest tube drainage and antibiotic therapy with early operative management if clinical improvement is not evident. Prospective studies addressing this issue are lacking [69].

Thoracoscopic decortication for empyema is best accomplished with lung isolation. This not only provides the most optimal surgical exposure but also helps to minimize contamination of the nonoperative side. Ho and Tobias have described the use of the Arndt blocker for this purpose [70, 71]. Ho et al. [72] also described the use of a tracheal tube exchanger to facilitate intermittent bronchial intubation when using a single-lumen tube for lung isolation. The tube exchanger is inserted in the mainstem bronchus of the nonoperative lung and the tracheal tube is railroaded over the exchanger. When periodic reexpansion of the operative lung is desired the ETT is withdrawn along the tube exchanger into the trachea. The tube exchanger acts as a guide to revert to one-lung ventilation as needed.

Untreated empyema develops a thick fibrinous plaque that does not permit collapse of the affected lung. In these patients, decortication is almost always warranted. Anesthetic monitoring of these patients may include an arterial line as well as conventional noninvasive monitors. As blood transfusion may

occasionally be required, adequate venous access is essential. Induction of anesthesia is usually not complicated, although these patients may have significant respiratory distress. With single-lung ventilation established, a pulmonary recruitment maneuver (sustained CPAP for a few seconds) may be beneficial prior to final positioning. This maneuver will have to be repeated at the request of the surgeon to reexpand the nondependent lung.

In most cases, tracheal extubation and transfer to a monitored ward bed is sufficient, however these patients rarely require postoperative ventilation. Intravenous antibiotic therapy should be continued.

Patent Ductus Arteriosus (PDA)

Surgical PDA repair is perhaps the most common cardiac procedure to be managed by the noncardiac specialized pediatric anesthesiologist. As technology and surgical technique have evolved, so too has the surgical management of this disease. The historic use of a large lateral thoracotomy has today been replaced by smaller muscle sparing “mini” thoracotomies. Moreover, many centers have established good success rates with the VATS technique [60, 73]. Percutaneous coiling of the PDA via interventional angiography is also widely available but will not be discussed herein [74, 75].

The ductus arteriosus is an essential conduit directing blood flow away from the high pressure pulmonary circulation toward the systemic circulation during fetal development. It most often arises at the anterior surface of the main PA and attaches to the descending aorta near the left subclavian artery. In response to the increased PaO_2 after birth, the musculature of the ductus constricts and effectively closes the structure. Smaller birth weight infants and premature infants are more likely to have persistently PDA. If left untreated the left-to-right shunt created by the PDA will result in pulmonary overcirculation, pulmonary edema, and respiratory insufficiency. RV failure may also develop, especially if pulmonary pressures increase. Rarely, this may result in shunt reversal. In children who have a hemodynamically stable PDA, closure is still required as the risk of bacterial endocarditis is quite high [76].

If significant pulmonary overcirculation exists the patient may require tracheal intubation in NICU to help support ventilation prior to surgery. These patients may often be fluid restricted and given diuretics in order to help alleviate the resultant pulmonary valvular insufficiency. To this end, inotropic support will also occasionally be required. Surgical stress will further strain the already compromised preexisting respiratory and hemodynamic status. Likewise, any preexisting medical condition or syndrome should be evaluated prior to induction of anesthesia. Whether performed via mini thoracotomy or VATS, surgical closure of a PDA is usually of short duration (<1 h typically) and involves minimal blood loss. In order to assess the blood flow in both the ascending (preductal) and descending (postductal) aorta, a noninvasive blood pressure cuff may be placed on a lower limb with an

oxygen saturation probe applied to both the right hand and the left foot. Invasive arterial measurement is no longer routinely required. When identification of the PDA is difficult the surgeon may place temporary clips across the vascular structure and observe the effects on the patient. Correct positioning across the PDA will result in a rise in diastolic pressures, whereas occlusion of the main PA will result in decreased oxygen saturation and ETCO_2 . Temporary occlusion of the descending aorta will result in a sudden loss of lower extremity saturation tracing and blood pressure while simultaneously preserving the preductal saturation.

Induction of anesthesia is dependent on the preexisting condition of the patient. Those that present with respiratory or hemodynamic compromise may typically receive a high dose narcotic (e.g., fentanyl 10–20 $\mu\text{g}/\text{kg}$ IV) at induction with muscle paralysis. Minimal volatile anesthetics should be used in these cases and supplemental narcotic dosing may be given as required. Alternatively, a remifentanil infusion along with low volatile anesthetic concentration may be used in those patients suitable for postoperative tracheal extubation. In addition to the standard intravenous used for induction, a larger peripheral intravenous catheter should be inserted after induction. Blood should be available in the operating theater for fluid resuscitation in the event of surgical misadventure. Open thoracotomy for PDA closure does not require lung isolation or single-lung ventilation. Simple retraction is sufficient to provide surgical exposure. Recent studies, however, have shown the efficacy of the VATS approach to PDA repair [77–80]. Ventilatory strategies for this include lung isolation (by any technique described earlier) or placement of a single-lumen ETT and allowing the pneumothorax to dictate surgical exposure. Muraldihar et al. [81] evaluated right mainstem bronchial intubation vs. low tidal volume-high frequency ventilation of both lungs and showed more profound desaturation in the mainstem intubated patients. Miyagi et al. [82] reported on the successful use of the Fogarty catheter as a bronchial blocker for a series of PDA closures performed via VATS. Despite the potential for hemorrhage, many studies have shown the safety and efficacy of this surgical approach for the repair of PDA [62, 66]. Risk factors, regardless of approach, continue to be hemorrhage, residual patency, and recurrent laryngeal nerve injury. Odegard et al. [83] describe a simple yet effective means to identify the recurrent laryngeal nerve and thus prevent injury during VATS procedures by using a thin Teflon nerve stimulating probe and recording the evoked electromyograms.

Tracheoesophageal Fistula (TEF)

The incidence of TEF is approximately 1 in 3,000 and although it may occur in isolation, about 50% of cases will present in association with other congenital anomalies [84]. The VACTERL association (vertebral, anal and cardiovascular defects, TEF, renal and radial limb defects) has been well described [85, 86]. The most commonly associated cardiac defects are atrial septal defect, PDA, and tetralogy of Fallot [87]. Investigation of

these defects is essential prior to any surgical intervention. The trachea and esophagus are derived from the primitive foregut during the fourth and fifth weeks of life. The trachea emerges ventrally from the primitive foregut and a septum between the esophagus and trachea is created by fusion of the tracheoesophageal folds. Failure of incomplete separation of these two structures can result in isolated esophageal atresia (rare) or more commonly TEF. The Gross classification describes six of the most common forms of TEF [88]. Type C, accounting for 85% of all cases of TEF, consists of a fistula located slightly above the carina with proximal esophageal atresia. It is suggested shortly after birth with copious salivation associated with choking, coughing, and cyanosis coincident with the onset of feeding. Diagnosis is confirmed by the inability to pass a suction catheter into the stomach and a gastric air bubble is often visible on radiograph. In most patients, surgical intervention will be planned for within the first week of life. During this time, these patients should be kept in a head-up or lateral decubitus position with a nasoesophageal suction catheter inserted to help prevent aspiration. Early tracheal intubation is rarely required. In otherwise healthy newborn infants, there is almost 100% survivability. Survival declines rapidly if TEF is associated with low birth weight, prematurity, cardiac anomalies, or pulmonary complications [75, 89].

Primary repair consists of fistula ligation and esophageal anastomosis. Occasionally, a staged repair will be required in patients that are unstable, premature, or have very low birth weight. This consists of placement of a balloon tip catheter into the distal esophagus via percutaneous gastrostomy under local anesthesia [90]. This temporizing measure helps prevent reflux and will enable more efficient ventilation, particularly if high airway pressures are required. When the patient becomes more stable the definitive repair can be performed. This has traditionally been undertaken through a thoracotomy on the side opposite the aortic arch. Fistula ligation is followed by esophageal anastomosis. If the two ends of the esophagus are separated by too great a distance the fistula is ligated and a section of colon can be interposed at a later date. Thoracoscopic repair has been described and in some centers it has become the preferred surgical approach [91, 92].

Anesthetic management begins with the understanding that positive pressure ventilation should be minimized on induction. If the fistula is large, pressurized gas flow will follow the path of least resistance through the fistula and into the stomach. This will cause gastric dilatation leading to further impairment of ventilation and possible reflux of gastric contents into the lungs. Profound respiratory failure and cardiac arrest have been reported. The goal of induction is to place the ETT distal to the fistula and proximal to the carina. This is often accomplished by blind mainstem intubation and subsequent retraction of the ETT until bilateral breath sounds are auscultated. Some centers advocate initial rigid bronchoscopy with the patient breathing spontaneously under volatile or intravenous anesthesia in order to identify the size and location of the fistula prior to tracheal intubation. Flexible

fiberoptic bronchoscopy may also be used to verify tube positioning following tracheal intubation. Prior to induction the patient should have thorough suctioning of the esophageal catheter and be well preoxygenated. Pretreatment with atropine is recommended. Traditionally, an awake tracheal intubation would have been performed on these patients. More recently, pediatric anesthesiologists prefer to induce anesthesia with inhaled volatile anesthetic while maintaining spontaneous respiration or alternatively, perform a rapid sequence induction. Once the ETT is carefully positioned to ensure lung ventilation without fistula insufflation, muscle relaxation and gentle positive pressure can be provided. Some anesthesiologists will prefer not to paralyze or provide positive pressure ventilation until the fistula is ligated. For thoracoscopic TEF repair lung isolation is generally not attempted. Anesthetic induction and tracheal tube placement is as for open repair, however maintaining spontaneous respiration until the fistula is ligated is impractical. The induced pneumothorax/capnotherax often produces adequate surgical exposure.

Intraoperative monitoring consists of the usual noninvasive monitors and possibly an arterial line. A large peripheral intravenous for fluid resuscitation should be obtained. A precordial stethoscope placed in the left axilla will help identify movement of the ETT into the right mainstem bronchus. The flexible fiberoptic bronchoscope should be available as it may be required to confirm intraoperative tube placement. Tracheal suction catheters should be on hand as surgical manipulation of the nondependent lung may cause debris or secretions to obstruct the ETT.

Intraoperative complications usually consist of ventilation difficulties, leading to hypoxemia and/or hypercapnia. Increasing FiO_2 , adjusting ventilatory settings, and providing muscle relaxation may help improve this. Occasionally, and more commonly during thoracoscopic procedures, a degree of hypercapnia and desaturation must be tolerated. Although some of the most robust patients may be suitable for postoperative tracheal extubation, most will benefit from a short period of elective ventilation. The tracheal tube is carefully withdrawn to a position proximal to the fistula and the non-dependent lung is gently reexpanded under direct vision. The hemithorax is simultaneously filled with warmed saline to ensure there is no air leak from the repaired fistula site. Early postoperative complications include atelectasis, increased airway secretions causing small airway collapse, and electrolyte disturbances associated with increased fluid requirements. Later complications include esophageal anastomotic leak, formation of broncho-esophageal fistula, and esophageal stricture formation [93].

Mediastinal Mass

Management of the pediatric patient with a mediastinal mass presents unique and serious challenges to the anesthesiologist. A common misconception is that a mediastinal mass is more likely to cause symptoms in children compared to adults [94].

In fact children are less likely to be symptomatic compared to an adult [95–97]. The presence of symptoms may be predictive of malignancy in the adult; however, this does not seem to hold true for children [98]. A finding of orthopnea (supine dyspnea) in the child may be predictive of significant tracheal narrowing [99, 100], and its presence should alert the clinician to the possibility of airway obstruction upon induction of anesthesia. The presence and degree of orthopnea should be assessed in every patient. The older child with mild symptoms can lie supine with some cough or pressure sensation. The patient with moderate symptoms will only be able to lie supine for short periods, and the severely symptomatic patient will not tolerate the supine position [101]. Characterizing the degree of orthopnea in the infant or small child is more challenging. The infant without symptoms will not seem stressed when supine, whereas the mildly symptomatic infant may look frightened or upset when supine. It is difficult and of little clinical use to attempt to distinguish between moderate or severe symptoms in the small child or infant. In either case, the infant will look severely distressed, may be gasping, or even cyanotic when supine.

Despite the predictive value of orthopnea in older children with a mediastinal mass, life-threatening complications may occur in the absence of symptoms, particularly in infants and small children [102].

The other major complication is cardiovascular collapse secondary to compression of the heart or major vessels. The presence of a pericardial effusion is associated with an increased risk of cardiovascular complications during anesthesia [103]. Death upon induction of general anesthesia in patients with an anterior mediastinal mass is always a risk. Anesthetic deaths have mainly been reported in children [104]. This may be due to the fact that:

1. Children have a more compressible cartilaginous airway structure.
2. The presenting signs and symptoms correlate poorly with tumor size.
3. Children are less able to give a reliable history.
4. Children more often receive a general anesthetic for tissue biopsy.

Diagnosis and Risk Stratification

The most important diagnostic test in the patient with a mediastinal mass is CT of the trachea and chest. Although a chest X-ray is often helpful in detecting a mediastinal mass, the CT scan provides useful information such as the size and compressive effects of the mass. For proper tumor staging however, a CT scan of the chest, abdomen, and pelvis is required. Fortunately, this can be accomplished with an average scan time of under 20 s with the more modern, faster CT scanners. In addition, the patient's head and chest can be elevated to 30° without affecting scan quality. Alternatively, the scan can be done with the patient in lateral or even prone position, if necessary.

It is essential to determine the patient's most comfortable position prior to starting the CT scan. Most patients, including the otherwise uncooperative child, will often assume that position while confined to the hospital bed. Furthermore, many major pediatric centers have adopted the resourceful practice of performing the scan at a time that coincides with that child's natural sleep. Distraction (with music or video) has been used with success in older children. For practical purposes, this means that the scan can be done with the patient in his/her most comfortable position during natural sleep, thus minimizing the need for sedation. The anesthesiologist should never feel compelled to have the severely symptomatic patient lay flat and supine, be deeply sedated, or anesthetized for a CT scan. In such a situation, if the above measures are unsuccessful or impractical, serious consideration should be given to steroid administration or selective irradiation prior to CT in order to reduce the tumor mass.

For those patients that are uncooperative but do not have severe symptoms, sedation may be administered, provided a cautious approach is adopted. Although nothing is absolute, careful titration of a single agent may be safer or preferable to polypharmacy, particularly for small children. A 6-year review of over sixteen thousand sedations performed on children revealed that the odds of having an adverse event were nearly 5 times higher when multiple agents were used (odds ratio [OR] 4.9, 95% CI 2.9–8.4) [105]. As a single agent, nitrous oxide 50% in oxygen is often all that is needed in small children to provide analgesia and sedation. Alternatively, midazolam or etomidate 0.1 mg/kg, ketamine or propofol 0.25 mg/kg IV boluses, or continuous infusion may be carefully titrated to effect. Although many agree that the risk of airway obstruction and hypoxemia increases when a combination of benzodiazepines and opioids is used [106], sedation even with a single agent may not be tolerated in the high risk patient [107]. Of equal importance is appropriate monitoring of the patient, early recognition and treatment of complications, and attention to patient positioning during the procedure. The flat, supine position is never mandatory.

Obstruction of the superior vena cava (SVC) causing venous hypertension and engorgement of venous collaterals leading to cyanosis and edema of head, neck, and upper extremities is known as the SVC syndrome [108]. The most common cause of SVC syndrome in children is primary lymphoma or lymphoblastic leukemia [109]. SVC syndrome is often present without associated airway compromise in the adult with a mediastinal mass. In children with such a mass however, the SVC syndrome is closely associated with and may predict the development of acute airway compromise. Tracheal intubation may be more difficult due to laryngeal edema that results from SVC obstruction. This obstruction may also cause pulmonary artery or myocardial compression, or affect right ventricular output, causing right heart failure [110]. Anesthetic-induced myocardial depression will aggravate these effects, with potentially disastrous consequences. Cerebral venous drainage and cerebral perfusion pressure may also be reduced in the

patient with significant SVC obstruction. As such, any patient presenting with SVC syndrome should be considered high risk. Patients with cardiovascular symptoms, SVC syndrome, or those patients unable to give an adequate history should therefore have transthoracic echocardiography to assess for cardiac, systemic, or pulmonary vascular compression.

Historically, children with tracheobronchial compression greater than 50% on CT have been considered high risk for general anesthesia [111]. More recent reviews have found the presence of orthopnea or SVC syndrome may be predictive of anesthesia-related complications [107, 110], but the extent of symptoms do not correlate well with the degree of tracheal narrowing on CT scan [99]. Based on these studies and the authors' clinical experience, the following risk stratification guideline regarding safety for general anesthesia is suggested. The patient with minimal to no orthopnea and near normal tracheobronchial area on CT scan will likely tolerate general anesthesia. In contrast, the child with moderate to severe orthopnea, tracheobronchial area <50% of normal on CT scan, or the patient with evidence of SVC syndrome or a pericardial effusion should be considered high risk. Unfortunately, there are several patient groups whose risk for general anesthesia remains uncertain. They include the child with mild orthopnea whose tracheobronchial diameter is unknown, and older child who is unable to give a history.

Direct examination of mediastinal mass tissue has been the traditional and preferable approach to making the diagnosis. In high risk or symptomatic patients however, the risk of general anesthesia and thoracotomy, mediastinoscopy, or VATS may be considerable. Excisional biopsy of extrathoracic lymph nodes has often been sufficient to confirm the diagnosis and allow for appropriate therapy. Increasingly, cytometric and immunocytochemical studies of pleural fluid have also been used with success to secure a diagnosis, obviating the need to deliver deep sedation or general anesthesia. Thoracentesis is particularly useful in lymphoblastic lymphoma, which is associated with a high incidence of pleural effusion [112, 113].

In the high risk patient without extrathoracic lymphadenopathy or a pleural effusion, percutaneous needle biopsy of the tumor under ultrasound or CT guidance may be a safe alternative [114, 115]. In centers equipped with interventional radiology expertise, core needle biopsies can be obtained under ultrasound guidance with the patient in a semi-upright or lateral position [116, 117]. This can be achieved under local anesthesia and mild sedation as required. The most obvious disadvantage to needle biopsy is the inherent "failure to diagnose" rate due to insufficient tissue for complete histological and molecular classification, although a failure rate exists also for open biopsy [118].

The use of prebiopsy corticosteroid treatment to reduce tumor size has generally been avoided if possible due to the extreme and rapid responsiveness to this (and radiation) therapy. There is widespread belief that prebiopsy steroid therapy will impair accurate histological diagnosis and result in suboptimal treatment or recurrence with a less favorable prognosis.

A 10-year review of children presenting with an anterior mediastinal tumor sheds light on and refutes this myth [119]. Twenty-three of the 86 patients in that series received prebiopsy hydrocortisone because of clinical evidence of respiratory compromise. Prebiopsy steroid treatment was felt to have had an adverse effect on the pathological diagnosis in five of the 23 children, however survival in those five patients was unaffected, and the authors concluded that prebiopsy steroid administration is defensible in symptomatic patients. In a more recent series, one third of children with a mediastinal mass were treated with corticosteroids prior to diagnosis because they were considered high risk. A clear diagnosis was made in 95% of these patients despite steroid therapy [102]. In these cases, close and ongoing consultation with the oncologist is essential. Prebiopsy steroid therapy may be justifiable (and arguably necessary) if the patient has symptoms and CT evidence of significant airway or cardiovascular compression, and is too young or uncooperative to tolerate local anesthetic alone. A typical regimen consists of 20-mg prednisone equivalents per meter square of body surface area, administered 3 times daily. Coordination between the oncologist, surgeon, and anesthesiologist is essential as biopsy tissue should be obtained between 12 and 24 h after starting steroid therapy. These patients should be monitored and treated in anticipation of developing tumor lysis syndrome, a constellation of metabolic abnormalities which can include hyperkalemia, hyperuricemia, hyperphosphatemia, secondary hypocalcemia, and acute renal failure [120].

Another alternative to preoperative steroids in the high risk patient includes irradiating the tumor while leaving a small area covered with lead for subsequent biopsy. This is not a viable option for the majority of pediatric patients presenting with a mediastinal mass as it requires the patient be cooperative and able to lie still for the duration of the treatment.

Flow-volume loops are commonly ordered as part of the preoperative assessment for patients with an anterior mediastinal mass. Specifically, the development of an increased expiratory plateau when changing from the upright to the supine position is thought to be pathognomonic for a variable intrathoracic airway obstruction and an indicator of patients who are at risk for airway collapse during induction of anesthesia. However, a careful examination of the literature reveals that this emphasis on flow-volume loops derives from a single case report [121]. Apart from isolated case reports, studies of flow-volume loops have shown a poor correlation with the degree of airway obstruction [122–124]. The use of flow-volume loops in the assessment of patients with anterior mediastinal masses is well described in standard anesthesia texts and frequently asked on anesthesia specialty exams. However in clinical practice, it is difficult to see how flow-volume loops add any useful information beyond that which is obtained from the history and chest imaging. Certainly flow-volume loops may show some correlation with airway obstruction in selected patients. However, modern chest imaging will tell the clinician not only if there is an obstruction,

but also its location, severity, and extent. This is the truly vital information in deciding how to manage the airway of a patient with an anterior mediastinal mass.

Although deep general anesthesia and muscle relaxation can be avoided in most patients with symptomatic lesions, invariably the anesthesiologist will be faced with the uncooperative child with a compressive mediastinal mass requiring general anesthesia for a diagnostic or therapeutic procedure. Management of these patients is guided by their symptoms and the CT scan. A stepwise induction of anesthesia with continuous monitoring of gas exchange and hemodynamics is recommended. This may be achieved by inhalation of a volatile agent such as sevoflurane or IV titration of propofol or ketamine, which maintains spontaneous ventilation until either the airway is definitively secured or the procedure is completed [125]. Awake intubation of the trachea before induction is a possibility only in older, mature pediatric patients if the CT scan shows a distal area of noncompressed trachea to which the ETT can be advanced before induction. If muscle relaxation is required, ventilation should first be gradually taken over manually to assure that positive-pressure ventilation is possible and only then can a muscle relaxant be administered. In some centers, muscle relaxation is avoided throughout the entire procedure if at all possible, as there have been cases of cardiorespiratory collapse that were likely caused by the resultant loss of muscle tone [126].

Airway or vascular compression can develop at any stage of the procedure and should be anticipated. In the preoperative assessment, the patient will often report that there is one side or position that causes less symptoms of compression. This, along with the findings on chest imaging, should be communicated to the entire operative team prior to anesthetic induction. In the event of intraoperative life-threatening airway or cardiovascular collapse, the patient should immediately be placed in that predetermined position, which will often result in a dramatic clinical improvement. The prone position has also been lifesaving in this setting [127]. Rigid bronchoscopy and ventilation distal to the obstruction may be necessary. As such, an experienced bronchoscopist and rigid bronchoscopy equipment must always be immediately available. In emergent situations, it is often not possible to push a standard ETT distally through the collapsed trachea. Ventilation and oxygenation can be reestablished temporarily with either a ventilating rigid bronchoscope or with jet ventilation via a rigid scope. Ultimately a reinforced ETT should be placed distal to the obstruction to stent the airway. This can be done by passing an airway exchange catheter or bougie distally under direct vision through the rigid bronchoscope, then withdrawing the bronchoscope and using the airway catheter as a guide for the ETT [128]. In fact it may be reasonable to use an armored tube in all patients with a mediastinal mass; however, a stylet will still be needed to advance the tube distal to the compressed portion of the airway. Depending on the response to the above emergency measures, the patient may have to be awakened as rapidly as possible and other options for surgery explored.

Heliox may be used in the event of subtotal airway collapse to decrease the work of breathing. Heliox is a mixture of helium and oxygen (most commonly 70:30) and decreases the turbulent airflow resistance through a narrowed airway due to the decreased density of helium.

Femorofemoral cardiopulmonary bypass (CPB) before induction of anesthesia is a possibility for older and more cooperative children who are considered “unsafe” for general anesthesia. Although emergency percutaneous CPB has been used successfully in an adult patient with impending complete airway obstruction [129] this is not a practical option in the young, frightened child. In addition, even the smallest femoral bypass cannulae are too large in diameter to be used in the patient weighing less than 15–20 kg. In such a case, preoperative steroid therapy should be considered.

The concept of CPB “standby” during attempted induction of anesthesia is fraught with danger because there is not enough time after sudden airway collapse to establish CPB before hypoxic cerebral injury occurs. It is not a practical option in the pediatric patient with a large anterior mediastinal mass. For patients who present with primarily cardiovascular rather than airway compression, rigid bronchoscopy will not be a useful resuscitation maneuver in the event of cardiovascular collapse. Resuscitation intraoperatively may require emergent sternotomy and lifting the tumor off the heart and great vessels [130]. For this reason, whenever possible, patients with cardiovascular compression should be prepped and draped for surgery prior to induction of anesthesia.

Congenital Diaphragmatic Hernia (CDH)

Congenital herniation of the abdominal contents into the thoracic cavity occurs in approximately 1 in every 2,500 live births [131]. The majority of cases will present prenatally if the mother has undergone standard ultrasonography [132, 133]. Occasionally, the diagnosis will be made in the early postnatal period. Intrusion of abdominal viscera into the thorax during fetal lung development leads to pulmonary hypoplasia and pulmonary vascular hypertension. This may promote persistence of fetal circulation (i.e., patent foramen ovale and PDA) after birth. Most cases of CDH occur on the left side at the Foramen of Bochdalek, accounting for 80% of unilateral herniations. Less common is herniation at the Foramen of Morgagni or at the esophageal hiatus itself. Mortality is related to the size of the defect and the association of cardiovascular anomalies. Approximately 10–30% of patients with CDH will have other congenital anomalies. These include congenital cardiac disease, chromosomal abnormalities (e.g., trisomy 18 and 21), CNS (e.g., spina bifida, hydrocephalus), and gastrointestinal anomalies (e.g., TEF, malrotation, atresia) [134]. Right-sided hernias are more often associated with these other defects. Large diaphragmatic hernias not diagnosed prenatally will present at delivery with severe respiratory distress and cyanosis. Physical findings include decreased breath sounds unilaterally or bilaterally. Indrawing, nasal flaring, and accessory

muscle use indicate impending respiratory failure. Palpation of the trachea often reveals deviation away from the affected side. Peristaltic (bowel) sounds may be heard over the affected hemithorax. Chest X-ray will reveal mediastinal shift away from the affected hemithorax as well as air filled bowel loops in the chest. The position of a nasogastric tube will be above the diaphragm.

As a result of compression and interference with normal lung development, the affected lung is reduced in volume and hypoplastic. Pulmonary surfactant deficiency contributes to poor lung compliance. This results in poor gas exchange and worsening of hypoxia, hypercapnia, and acidosis. PVR may remain elevated with persistent fetal circulation. High airway pressures and hemodynamic instability can further drive pulmonary hypertension. With elevated PVR and a PDA right-to-left shunting will occur. Other sites of shunting may also exist depending on the associated cardiac pathology. Systemic hypoxia will continue because of this shunting and disease progression will accelerate. Without appropriate preoperative support this cascade of hypoxia, acidosis, increasing PVR, and right-to-left shunt will lead to cardiac dysfunction and patient demise.

Management strategies for CDH have changed over the last few decades [83, 135]. Currently, preoperative stabilization followed by early surgical repair is recommended. Much of the recent work has focused on optimizing hemodynamic and ventilatory support in this patient population [136]. At present no one best strategy has been universally agreed upon. Historically, resuscitative efforts were aimed at achieving alkalosis through active hyperventilation with the goal of minimizing pulmonary vascular hypertension. Contemporary “gentle” ventilation guidelines aim to minimize barotrauma by limiting maximal inspiratory pressures and tidal volumes. Much like in the management of adult RSD a degree of hypoxia and hypercapnia is accepted. Survivability has actually been shown to improve in these patients managed in this way provided PaO_2 is kept at 60 mmHg and PaCO_2 approaches 65 mmHg [137–139]. Until invasive arterial vascular access can be gained, one may aim for a preductal oxygen saturation of 85% with postductal saturation of 60%. Failure to achieve these goals with conventional ventilation may be an indication for conversion to high frequency oscillatory (HFO) or jet ventilation. To facilitate this method of ventilation judicious use of sedatives, narcotics, and muscle relaxants will be required. Alternatively, progressive hypercapnia and acidosis with an A-a gradient >500 mmHg are indications for ECMO [140, 141].

Pharmacologic adjuncts for the management of pulmonary hypertension have included inhaled nitric oxide, sildenafil, prostaglandins, and prostacyclins [142]. In this case, inotropic support is often required. The overall mortality rate for CDH still remains quite high (greater than 50%) despite improved prenatal detection, transfer to tertiary institutions for delivery, and advances in neonatal care [143].

The anesthesiologist may first become involved during resuscitative efforts at the time of birth. Early insertion of a

nasogastric tube will be necessary to decompress the stomach. The reduced volume of air in the stomach will aid ventilatory mechanics. Likewise bag mask ventilation should be kept to a minimum to avoid further gastric distension. If oxygen saturation continues to decrease despite NG tube insertion and high flow oxygen then tracheal intubation is appropriate. Sedatives, narcotics, and muscle relaxants are often administered to facilitate tracheal intubation and positive pressure ventilation.

Intraoperatively the anesthesiologist must attempt to maintain ventilation and oxygenation as discussed earlier. Conversion from HFO to conventional ventilation should be attempted prior to surgery, although CDH repair is possible with the patient on HFO ventilation [144, 145]. Peak airway pressures should be limited to avoid barotrauma and worsening PVR. A sudden rise in airway pressures or decrease in lung compliance can indicate a contralateral pneumothorax which must be diagnosed and treated promptly as it may be associated with a worse outcome. Anesthetic management typically includes a narcotic and muscle relaxant technique. In addition to basic monitoring an arterial line (preferably right radial) as well as pre and postductal oxygen saturation monitors should be placed. Decreasing postductal saturation may indicate worsening right to left shunt and increasing PVR. Closure of the diaphragmatic hernia may compromise venous return from the lower extremities and therefore intravenous access in the upper limbs is preferred. Insertion of an internal jugular venous line is not essential and risks causing a pneumothorax, but if already present can be a useful adjunct for monitoring right-sided pressures and venous oxygen saturation.

Surgery usually consists of an abdominal incision with the herniated contents being reduced into the abdomen. Small defects can then be closed primarily while larger ones may require the use of a synthetic patch. Closure of the abdomen may also necessitate the use of a patch to avoid cardiopulmonary compromise in the event of elevated abdominal pressures. With reduction complete, the hypoplastic lung should not be aggressively ventilated as this will increase the risk of barotrauma, contralateral pneumothorax and is typically of little or no therapeutic value. Thoracoscopic repair of CDH has been described in the pediatric population with good outcome [146, 147]. A prospective comparison of the open abdominal approach vs. VATS has not been conducted. Trocar insertion is carried out with the patient in the lateral decubitus position and minimal CO_2 insufflation pressures are used (i.e., 2–4 mmHg). The hernia contents are pushed down into the abdomen and the defect closed. An ipsilateral chest tube is also placed. Lung isolation is not required. Postoperative intensive care monitoring is required for all CDH patients and most will require a period of postoperative ventilation.

Lung Biopsy

Optimum management of solid lung masses almost always requires correct pathological diagnosis via biopsy of the

affected tissue. Obtaining such samples, however, can be challenging, especially when dealing with pediatric patients. The traditional method for acquiring these samples has been open lung biopsy, which is associated with morbidity and considerable pain. Increasingly, less invasive procedures such as endobronchial biopsy and image-guided percutaneous biopsy have been used in children [148]. Concerns regarding endobronchial biopsy include bleeding and the histologic adequacy of the sample obtained. Minor mucosal bleeding is common and not of great concern as experience with airway foreign body removal would indicate that minor bleeding of the mucosa is not associated with a worse outcome [149]. Although not all lung masses are accessible via transbronchial biopsy, it is useful as a diagnostic measure in patients with poorly controlled asthma [150], cystic fibrosis (CF) [151, 152], and postlung transplant monitoring [153]. Salva et al. [54] prospectively studied 170 children between the ages of 2.5 and 16 years who underwent flexible endobronchial biopsy for a variety of chronic respiratory conditions. At least three biopsy samples were taken from each patient. These children received a general anesthetic in an ambulatory setting with the use of an LMA (as described earlier). The results were encouraging as no patient required intervention for mucosal bleeding and there were no cases of pneumothorax, hemoptysis, or pneumonia.

Image-guided percutaneous lung biopsy can be performed with CT or ultrasound guidance depending on the location and accessibility of the tumor. Deep sedation with local anesthetic infiltration [154] or general anesthesia can be performed depending on age, cooperation, and medical status of the patient. Disadvantages compared to general anesthesia include the inability to suspend respiration to aide biopsy localization. In a series of CT-guided percutaneous lung biopsies performed in children between the ages of 0.6 and 20 years, most cases were performed successfully with deep sedation. Adequate tissue samples were obtained in 85% of the cases [155]. Perioperative complications that did not require intervention included subclinical pneumothorax (17%), pleural effusion (3%), subcutaneous hemorrhage (12%), and postprocedural hemoptysis (3%). There was one case of tension pneumothorax requiring chest tube insertion. There was no association between adverse events and the number of biopsy attempts. All children received a chest X-ray approximately 6 h after the procedure or sooner as clinically indicated. Despite an overall complication rate of 28%, percutaneous biopsy fares favorably when compared to historic data on surgical open biopsy. Procedure length, overall hospital stay, and procedural costs also tend to favor percutaneous biopsy.

For those patients in whom percutaneous biopsy has failed to yield a diagnosis and those in whom the lung pathology is not amenable to such a technique, surgical lung biopsy is required. This can be performed with open thoracotomy or VATS. Although postoperative morbidity is increased in comparison to percutaneous biopsy, surgical biopsy is still considered by many the gold standard diagnostic tool.

Gluer et al. [156] prospectively evaluated the feasibility, efficacy, and safety of the VATS technique for lung biopsy in patients with diffuse parenchymal lung disease. This was performed with general anesthesia using a single-lumen tube without lung isolation. The average age of the 21 patients was 3 years (range 12 days to 15 years). Only two cases required conversion from VATS to mini-thoracotomy and no other intraoperative complications were noted. Eight of the patients had a chest tube placed at closure (although no fixed criteria for placement were used). These were typically removed on the second postoperative day. One patient had persistent air leak requiring further surgical intervention. All biopsy samples were diagnostic. No data exists comparing the utility of VATS vs. thoracotomy for pediatric lung biopsy. Extrapolation from the adult experience would seem to suggest decreased postoperative pain, shorter hospital stay, and better cosmetic result with VATS. As experience with pediatric VATS procedures increases, we may see an increase in the number of biopsy procedures performed using this technique.

Cystic Fibrosis (CF)

Thick inspissated secretions causing airway obstruction, atelectasis, and superimposed pneumonia are some of the pulmonary sequelae of this multiorgan disease. Respiratory dysfunction can be quite pronounced with patients becoming extremely ill. Progression of the disease can lead to cor pulmonale, pneumothorax, antibiotic resistant infections, and bronchiectasis. Intestinal malabsorption, pancreatic and liver dysfunction are the most frequent extrapulmonary effects. Improved medical management, including chest physiotherapy, bronchodilators, antimicrobial treatments, and medications to break down secretions (i.e., Pulmozyme) have significantly improved outcome and quality of life for many patients. Despite this, eventual respiratory failure is the rule and, for many, lung transplant may be the only alternative. Children with CF may present for surgery at various stages of life. The neonate may present with meconium ileus or for central line placement for nutritional supplementation. Older children may present with pneumothorax requiring chest tube insertion and bronchoscopy for lavage of inspissated secretions and microbial diagnosis of infections can happen at any stage of life.

Anesthetic management is predicated on optimizing preoperative respiratory function. Consultation with the pulmonologist is indicated for all patients with CF. Medical management including appropriate antibiotic treatment, optimizing bronchodilator use, and initiating Pulmozyme therapy often requires the patient be admitted to hospital prior to the scheduled procedure. Preoperative laboratory investigations should include arterial blood gas, electrolyte panel, liver function tests, and blood glucose. Reviewing the most recent spirometry or PFTs and available chest imaging will also help in determining the degree of respiratory dysfunction. Chest physiotherapy for secretion clearance should be ordered preoperatively and early in the postoperative period. Controversy exists as to the most

favorable perioperative fluid management strategy. Although aggressive fluid supplementation may decrease the viscosity of pulmonary secretions, some anesthesiologists prefer to limit fluid administration to decrease the volume of secretions. To date no one best strategy has been found. Whichever approach is taken, it is advisable to have the patient euvoemic at the start of the procedure. Bronchoscopy, bronchoalveolar lavage, and transbronchial biopsies may be performed through an LMA with the patient breathing spontaneously, however, anesthetic depth must be sufficient to prevent coughing and laryngospasm. Increasingly, muscle relaxation and gentle positive pressure ventilation through the LMA has simplified anesthesia for bronchoscopic procedures in children with CF. If a tracheal tube is to be used it must be adequately large to allow for ventilation around the fiberoptic scope as well as tracheobronchial suctioning. Routine noninvasive monitoring is acceptable for straightforward procedures, however, an arterial line may be helpful in more involved cases to assess oxygenation, ventilation, and blood glucose monitoring.

Inhalational induction may be slow in patients with severe respiratory dysfunction and therefore intravenous induction is often preferred in this patient group. Intraoperative complications to be aware of include mucus plugging, pneumothorax, bronchospasm, and atelectasis. Inspired gases should be humidified and tracheobronchial suctioning should be performed at regular intervals throughout the procedure. Some clinicians advocate against the use of ketamine in children with CF as this drug can increase airway secretions. Regional techniques for pain management have the theoretical advantage of minimizing respiratory depression associated with systemic narcotic use and should be considered. In the mature child or teenager with CF undergoing peripheral surgery, regional anesthesia with or without mild sedation may be a reasonable option. A plan for postoperative ventilatory support must be discussed amongst the surgical team, anesthesia, intensivist, and the patient/family. Respiratory compromise due to surgery, postoperative sedation, narcotic analgesia, and a weakened cough will increase the likelihood of needing postoperative ventilator support.

Pulmonary Alveolar Proteinosis

PAP is a rare disease in which accumulation of phospholipoproteinaceous material in the alveoli causes pulmonary impairment [157]. A deficiency in granulocyte-macrophage colony-stimulating factor (GM-CSF) activity results in defective macrophages and reduced clearance of surfactant from the lungs [158]. Regular administration of GM-CSF as well as bronchoalveolar or whole lung lavage is an important part of treatment for this disease and often results in temporary improvement of symptoms and radiographic appearance (see also Chap. 35).

The small child with PAP requiring whole lung lavage presents a particular challenge to the anesthesiologist. In adolescents

and adults, double lumen bronchial tubes are often used to isolate the lungs for lavage, however such tubes do not currently exist for use in smaller children. Several techniques have been described to isolate the lungs in smaller children in order to allow for lavage. No single method has been shown to be ideal and each has its risks and limitations. Extracorporeal circulation has been used which allows for thorough bilateral whole lung lavage, however it is invasive and may be associated with significant morbidity [159]. Lavage through a flexible bronchoscope adjacent to a cuffed ETT allows for improved lung isolation [160]; however, this can be a lengthy process and also carries a risk of causing trauma to bronchial mucosa. Lavage through a pulmonary artery catheter has also been performed either through a rigid bronchoscope [161] or through an ETT [162]. This method also allows for lung isolation, however the diameter of a pulmonary artery catheter port is small and drainage may be inadequate. The most commonly used method of lung lavage in children is individual or multilobar lavage through a flexible fiberoptic bronchoscope. This may be performed through an ETT or an LMA. It is more time consuming than whole lung lavage, however, may be associated with lower lavage returns and does not isolate the lung.

For whole lung lavage in a child under the age of 9 years, true lung isolation may be achieved by using an assembly that mimics commercially available double-lumen tubes. Two cuffed tracheal tubes are passed through the glottis, one seated endobronchially to isolate the lung to be lavaged and the second seated in the trachea. These tubes are then connected to the angled and Y-connectors from a standard double lumen bronchial tube set (Fig. 39.6) [163]. Although this approach may allow for proper lung lavage, one-lung ventilation, and obviate the need for postprocedural ventilation, the nature of the underlying illness may nevertheless dictate the need for monitoring in a high acuity setting. Because of the nature of the procedure and the airway assembly, total intravenous anesthesia is likely preferable if this technique is to be used. This type of airway assembly can be used in the small child requiring differential lung ventilation and/or strict lung isolation for a variety of procedures other than lung lavage. Disadvantages include the necessarily smaller sizes of the two tracheal tubes needed to simultaneously pass through the vocal cords. Dexamethasone 0.1 mg/kg IV may be given prior to the procedure to reduce the risk of mucosal edema at the level of the cricoid cartilage.

Trauma, Pneumothorax, and Hemothorax

Due to the unique and changing physiology and psychology of children the management of the pediatric trauma patient may be quite different from that of the adult. Although isolated chest injuries are rare in children (5–15% of traumas), when associated with other injuries the mortality rate can be as high as 25% [164–166]. Between 60 and 80% of all pediatric trauma is blunt impact, usually from motor vehicle collision [108].

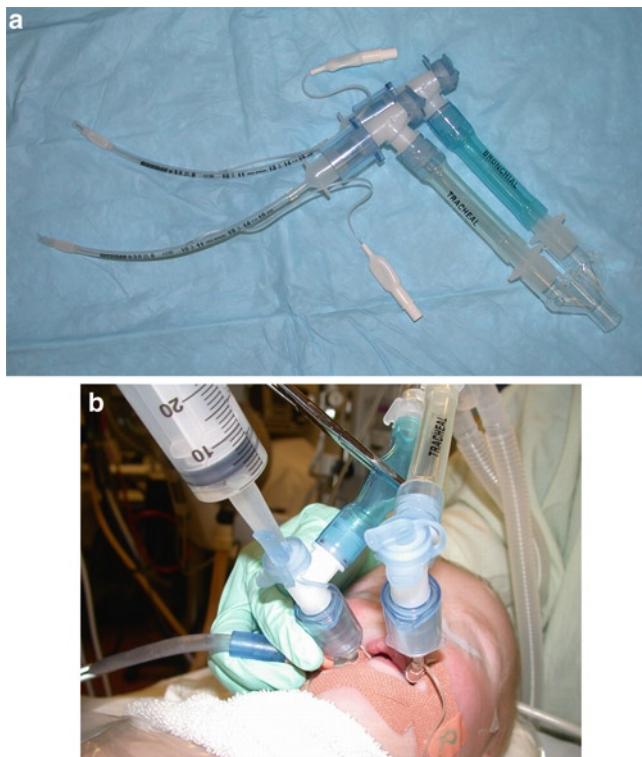


FIG. 39.6. (a) Airway assembly for use in the small child that mimics commercially available double-lumen bronchial tubes. Two cuffed tracheal tubes are passed through the glottis, one seated endobronchially to isolate the lung to be lavaged and the second seated in the trachea. These tubes are then connected to the angled and Y-connectors from a standard double-lumen bronchial tube set. (b) Whole lung lavage being performed in a 3-year-old child via the bronchial tube of the airway assembly while positive pressure ventilation is applied via the tracheal tube.

Incomplete ossification of the ribs in children means that the rib cage is more likely to deflect under traumatic assault as opposed to fracture. Therefore, pulmonary contusions are more likely in children as compared to adults even in the absence of overlying rib fractures [167]. Conversely, a child that presents with rib fractures has likely suffered a severe, high force trauma to the chest. Insertion of a thoracic epidural catheter should be considered in the analgesic management of the child with multiple rib fractures [168]. Penetrating chest injuries due to gun violence and knife stabbings are less common in children. The presence of rib fractures in the infant should raise suspicion of child abuse [169, 170].

Pulmonary contusion is perhaps the most common traumatic thoracic injury in the pediatric population [171, 172]. Within the lung parenchyma this manifests as alveolar edema and consolidation, sometimes associated with hemorrhage. Because of the child's higher metabolic oxygen consumption lung injury may be accompanied by significant hypoxemia. Mechanical ventilation may be required although most pulmonary contusions can be treated by less invasive

measures [173]. This includes BiPAP, supplemental oxygen, pain control, fluid restriction, and incentive spirometry when appropriate. Preventing and treating atelectasis is essential as this will reduce the risk of pneumonia and further respiratory compromise.

Pneumothorax may occur spontaneously in susceptible patients but is more often encountered at the conclusion of surgical thoracic procedures or in the setting of trauma. An open pneumothorax, one in which the pleura communicates with atmosphere, is treated with the insertion of a chest tube that allows for drainage without further entrainment of air upon inspiration. The chest tube apparatus is usually placed under water seal or to a suction device. Towards the end of most major thoracic procedures the surgeon will choose to electively place such a device. For minor intrathoracic procedures, some surgeons will elect not to place a chest tube. In these cases, air is removed as the chest wall is closed while the anesthesiologist provides positive pressure to the lung. These maneuvers should minimize any residual pneumothorax. A postoperative chest X-ray is required with careful monitoring of the patient for signs of increasing pneumothorax. Most small (i.e., <10%) pneumothoraces are insignificant and will resolve over a period of a few days.

Tension pneumothorax occurs when air accumulates in the pleural space without communicating with atmosphere. As the pressure builds within the pleural space the ipsilateral lung will further collapse with increasing mediastinal shift. Clinical deterioration of the patient will become apparent. Hypotension, hypoxia, and decreased cardiac output will require emergent management. Diagnosis is confirmed by decreased breath sounds on the ipsilateral side, tracheal deviation away from the affected lung, and shift of the maximal cardiac impulse. Radiographic diagnosis should not delay the emergent placement of a chest tube or needle decompression followed by chest tube insertion.

Bleeding into the pleural cavity can occur intraoperatively or postoperatively following any thoracic procedure. The amount of blood loss due to hemothorax in this setting should be minimal if hemostasis was achieved prior to closure. In the case of thoracic trauma, however, the amount of blood loss can quickly become life threatening. Disruption of intercostal arteries or veins is the most common culprit in this setting. As with tension pneumothorax, the accumulation of blood will compromise ventilation and cardiac output. If this blood is not promptly drained it may reorganize into a fibrous scar thus causing chronic atelectasis and V/Q mismatch. In addition to this, the blood may become a medium for bacterial growth with ensuing sepsis and empyema formation. Operative exploration of a hemothorax must be considered when there is ongoing drainage from the chest tube and/or the patient remains hemodynamically unstable. Some clinicians advocate a quantitative approach that would require surgical exploration if greater than 15 mL/kg of blood is recovered upon chest tube insertion or if ongoing drainage exceeds 4 mL/kg/h [174].

Major airway disruption is rare in pediatric trauma but may occur in the setting of penetrating injury or rapid acceleration or deceleration. When present these injuries can be immediately life threatening. In 80% of cases, the disruption is located at the distal trachea or main bronchus [175, 176]. Airway injury should be suspected in the setting of pneumomediastinum, subcutaneous emphysema, large persistent air leak within the chest tube, and frank respiratory collapse. Diagnosis is usually confirmed by bronchoscopy, either rigid or flexible. When airway injury is suspected, intubation should be performed fiberoptically and the ETT placed distal to the disruption to avoid further trauma or creation of a false passage. Immediate operative repair of major airway injuries may be required although minor injuries can be observed with delayed surgical repair as required. Distal injuries can be treated with simple resection while more proximal injuries may require quite extensive repairs. Postoperative complications may include dehiscence, airway stenosis, atelectasis, and pneumonia. A severe blow to the chest while the vocal cords are adducted can lead to a rare injury pattern that is unique to pediatrics. Traumatic asphyxia presents with neck and facial swelling and ecchymosis, subcutaneous emphysema, and pneumomediastinum [177]. The sudden increase in intrathoracic pressure causes a small tear in the upper trachea and forces air into the tissues of the neck, face, and around the mediastinum. Management is often supportive and non-surgical.

Lung Transplantation

Pediatric lung transplantation continues to account for a small fraction of all lung transplant operations performed. Despite this, the number of transplants performed on children is increasing and the minimum age of transplantation is decreasing. Many large pediatric transplant centers have established living donor programs and life-sustaining temporizing measures such as the Novalung® have been introduced for use in children awaiting a donor lung. The vast majority of pediatric lung transplant procedures are carried out in children between 10 and 17 years of age. CF accounts for over 64% of cases in children, followed by primary pulmonary hypertension (14%), pulmonary interstitial disease (7%), and retransplant (7%) [178]. Actuarial survival rates tend to be favorable for pediatric lung transplantation as compared to those for older adults.

A multidisciplinary team and approach is crucial to meet the surgical, medical, psychological, physical, and dietary challenges that will be faced. At the time of writing, children smaller than 10 years of age (i.e., those too small to accept a double lumen bronchial tube) usually undergo lung transplantation under cardiopulmonary bypass. Other indications for the use of bypass during lung pediatric transplantation include primary pulmonary hypertension and severe right ventricular dysfunction. There also continues to be a significant rate of

conversion from off-bypass double sequential lung transplant to urgent bypass in children due to worsening pulmonary hypertension or relentless hypoxemia. The advantage of off-bypass sequential lung transplantation is the avoidance of systemic anticoagulation needed for cardiopulmonary bypass. A short period of postoperative ventilation is provided to monitor for early complications such as ischemic–reperfusion injury, infection, acute rejection, bleeding, and anastomotic leaks.

Postoperative and Pain Management

The postoperative disposition of a child who has undergone a thoracic procedure will depend on many criteria including the type and length of surgery, extent of resection or manipulation, and nature of the underlying condition. In general, infants and small children will be more frequently managed with a short period of postoperative ventilation when compared to adult patients. This may be due to the increased fatigability of the infant's respiratory muscles or the fact that central neuraxial blockade is performed less often in small children than in adults. Occasionally surgical dehiscence is a concern in the early postoperative period and infants are less well able to tolerate the fluid shifts that often accompany extensive procedures. Regardless of the type of surgery or reason for intervention the pediatric patient should be monitored for respiratory status and adequate pain control in a suitable environment. Constant care or high acuity nursing and monitoring should be considered even if the patient's trachea was extubated in the operating room.

Because many procedures are now being done with the less invasive video-assisted thoracoscopic technique, postoperative pain management has become somewhat easier. These patients can often be managed with nonopioid analgesics, a simple narcotic infusion, or patient-controlled analgesia. Table 39.4 outlines commonly used analgesics in pediatric practice. Local anesthetic can also be infiltrated prior to the placement of trochars and multimodal analgesia should be considered in all patients. Pain control for the pediatric patient has recently regained a renaissance with the more aggressive use of regional anesthesia techniques. These techniques are being applied to a wider range of the pediatric population with good success and minimal complications. The proper management of postoperative pain can avoid some of the negative physiologic outcomes associated with poorly treated pain. These include heightened sympathetic drive, increased metabolism, decreased immune function and specifically for thoracic procedures, poor respiratory function [179]. A simple option for regional analgesia includes intercostal nerve blocks performed prior to skin incision or just before surgical closure under direct visualization. Local anesthetic dosages should be reduced as plasma uptake at this site is rapid [180]. The overlap of thoracic dermatomes requires that the nerves above and

TABLE 39.4. Commonly used analgesics in pediatric practice^a.

Analgesic	Dose ^b	Infusion dose (μ g/kg/min)	PCA dosing (μ g/kg q 6–10 min) or comment
Morphine	50 μ g/kg	10–40	10–30
Fentanyl	0.5 μ g/kg	0.5–2	0.2–0.5
Hydromorphone	0.15 μ g/kg	3–5	3–5
Remifentanil	0.5 μ g/kg	0.05–2	Intraoperative use only
Ketamine	0.15 μ g/kg	1–4	Narcotic sparing effect; may be useful if opioids side-effects considerable
Acetaminophen	75 mg/kg/day po	N/A	q4h dosing for oral, q6h for rectal
Ibuprofen	5–10 mg/kg po q6h	N/A	For children >6 months of age
Ketorolac	0.5 mg/kg (maximum 15 mg) q6h	N/A	For children >6 months of age. Limit to 48 h then switch to po ibuprofen

PCA patient controlled analgesia; po per os

^aAdapted from Sick Kids Acute Pain Handbook, 2010. The Hospital for Sick Children, Toronto, Canada

^bDoses are intravenous unless otherwise specified

TABLE 39.5. Neuraxial blocks and dosing guidelines suitable for pediatric thoracic procedures^a.

Type of block	Solution	Infusion rate (mL/kg/h)
Thoracic epidural ^b	0.125% bupivacaine + epi 1:400,000 \pm fentanyl 1–2 μ g/mL	0.1–0.16 maximum 10 mL/h
Thoracic epidural ^b	0.1% bupivacaine + epi 1:500,000 \pm fentanyl 1–2 μ g/mL	0.1–0.16 maximum 12 mL/h
Thoracic epidural ^b	0.0625% bupivacaine + epi 1:800,000 \pm fentanyl 1–2 μ g/mL	0.1–0.16 maximum 14 mL/h
Paravertebral ^c	0.125% bupivacaine + epi 1:400,000	0.2 maximum 15 mL/h
Intercostal ^d	0.125% bupivacaine + epi 1:400,000	0.016–0.032 per rib maximum 1 mL/h/rib
Intrapleural ^e	0.125% bupivacaine + epi 1:400,000	0.2–0.3 maximum 20 mL/h

^aAdapted from Sick Kids Acute Pain Handbook, 2010. The Hospital for Sick Children, Toronto, Canada

^bAlternatively, caudal or lumbar approach with epidural catheter threaded to thoracic level. Suggested loading dose of 0.2–0.25 mL/kg of 0.25% bupivacaine + epi 1:200,000 up to maximum 10 mL

^cSuggested loading dose of 0.3–0.5 mL/kg of 0.25% bupivacaine + epi 1:200,000 up to maximum 15 mL

^dSuggested loading dose of 0.05 mL/kg (maximum 2 mL) of 0.25% bupivacaine + epi 1:200,000 per intercostal space

^eSuggested loading dose of 0.2–0.3 mL/kg (maximum 20 mL) of 0.25% bupivacaine + epi 1:200,000

below the surgical site also be blocked. Indwelling intercostal catheters can also be placed by the surgeon and managed as a constant infusion postoperatively [181].

The epidural space in the child can be assessed in a similar fashion to that of adults. Ideally the epidural catheter tip should be placed at the dermatome level corresponding to the surgical site. Specific pediatric-sized Touhy needles should be used to minimize complications and provide for better control. Unlike in adults, thoracic epidural catheters are almost always placed when the child has already been anesthetized. Therefore, greater care must be exercised when advancing the needle as the patient will not be able to articulate the presence of radicular pain. Despite this drawback, there is no evidence to suggest the incidence of complications is higher in children compared to adults [182].

In smaller infants, the caudal epidural space can be easily accessed and a catheter advanced to the required thoracic level. Traditionally, this has been accomplished via electrical stimulation [183], although more recently an ultrasound-guided approach has become popularized [184]. As in adults many different local anesthetic solutions and adjuncts have been used in the pediatric population. The most commonly used local anesthetics continue to be Bupivacaine and Ropivacaine for either “single shot” or continuous infusion epidurals [185]. Suggested neuraxial blocks and dosing guidelines

suitable for pediatric thoracic procedures can be found in Table 39.5. Epidural narcotics are commonly coadministered as they reduce the dosage requirement for local anesthetics and improve the block quality. Epidural morphine, fentanyl, and hydromorphone are the most commonly prescribed narcotics for this use [186, 187]. The purpose of optimizing pain management strategies is not only to keep the child comfortable but also to avoid pulmonary dysfunction by enabling deep breathing and coughing. This can aide in the prevention of atelectasis and postoperative pneumonia. Early ambulation is also encouraged to further accelerate the recovery of the patient and prevent those diseases associated with prolonged immobilization and hospitalization.

Clinical Case Discussion

A 3-year-old child with a newly diagnosed left lung mass presents for tissue diagnosis followed 1 week later by thoracotomy and tumor resection.

The initial workup of the child will focus on the functional status and size of lung mass. Imaging will be essential to identify the size and location of tumor and to rule out a mediastinal mass. A CT scan will be required which may be done without sedation if the child is cooperative. Otherwise

a stepwise approach of cautious sedation may be required. Any sedation should be delayed to verify the absence of a significant mediastinal mass. Tissue samples may be obtained through a mini-thoracotomy, however, in tertiary pediatric centers image-guided needle core biopsy is preferred and associated with lower morbidity. Most 3 year olds will require deep sedation or general anesthesia. Spontaneous respiration can be maintained during the biopsies, which might be CT or ultrasound guided. Often tracheal intubation is not required and the patient's airway can be managed by face mask, bag-mask support, or insertion of an LMA. Sedation/anesthesia may be achieved by TIVA (propofol or ketamine, alone or in combination with a short-acting opioid or benzodiazepine) and/or inhalation. Occasionally, a brief period of apnea will be requested to facilitate biopsy. This may be achieved temporarily deepening the anesthetic and providing positive pressure ventilation. Postbiopsy X-ray should be performed to ensure there is no significant residual pneumothorax. Chest tube insertion is rarely required.

Tumor resection may be performed via VATS or open thoracotomy. In either case the anesthesiologist should be prepared to isolate the lung. Options in a 3-year-old include (1) selective right mainstem bronchus intubation with a 4.5- or 5.0-mm ID tracheal tube; (2) insertion of a size 5F embolectomy catheter in the left mainstem bronchus inside or (more practically) outside a 4.5-mm ID tracheal tube; or (3) a 5F Arndt Endobronchial blocker inserted in a 5.0-mm ID tracheal tube and placed in the left mainstem bronchus. Regardless of the option chosen, fiberoptic verification of proper tube or blocker positioning is crucial. A 2.2- or 2.8-mm OD pediatric fiberoptic bronchoscope should be used to ensure adequate ventilation may be provided while the scope occupies the lumen of the tracheal tube. The author prefers not to perform selective right mainstem bronchus intubations as quite often the tube slips distal to the right upper lobe takeoff, resulting in atelectasis of that lobe and worsening hypoxemia. Monitoring should include an invasive arterial blood pressure line in addition to standard monitors. Pain control will depend partly on whether VATS or open thoracotomy is performed. As a general guideline, central neuraxial blockade is offered in the event of open thoracotomy and systemic analgesics are administered if VATS is performed. Postoperative monitoring in a high acuity setting (step-down or critical care unit) is warranted for the first 12–24 h.

References

1. Sweet DG, Halliday HL. The use of surfactants in 2009. *Arch Dis Child Educ Pract Ed*. 2009;94(3):78–83.
2. Sekar KC, Corff KE. To tube or not to tube babies with respiratory distress syndrome. *J Perinatol*. 2009;29 Suppl 2:S68–72.
3. Verder H, Bohlin K, Kamper J, Lindwall R, Jonsson B. Nasal CPAP and surfactant for treatment of respiratory distress syndrome and prevention of bronchopulmonary dysplasia. *Acta Paediatr*. 2009;98(9):1400–8. Epub 2009 Jul 1.
4. Lista G, et al. Nasal continuous positive airway pressure (CPAP) versus bi-level nasal CPAP in preterm babies with respiratory distress syndrome: a randomised control trial. *Arch Dis Child Fetal Neonatal Ed*. 2010;95(2):F85–9.
5. Soll R, Ozek E. Multiple versus single doses of exogenous surfactant for the prevention or treatment of neonatal respiratory distress syndrome. *Cochrane Database Syst Rev*. 2009;(1):CD000141.
6. Cogo PE, et al. Dosing of porcine surfactant: effect on kinetics and gas exchange in respiratory distress syndrome. *Pediatrics*. 2009;124(5):e950–7. Epub 2009 Oct 12.
7. Suresh GK, Soll RF. Overview of surfactant replacement trials. *J Perinatol*. 2005;25 Suppl 2:S40–4.
8. Blaise G, et al. Pulmonary arterial hypertension pathophysiology and anesthetic approach. *Anesthesiology*. 2003;99:1415–32.
9. Hawkins A, Tulloh R. Treatment of pediatric pulmonary hypertension. *Vasc Health Risk Manag*. 2009;5(2):509–24. Epub 2009 Jun 7.
10. Konduri GG, Kim UO. Advances in the diagnosis and management of persistent pulmonary hypertension of the newborn. *Pediatr Clin N Am*. 2009;56(3):579–600, Table of Contents.
11. Knoderer CA, Morris JL, Ebenroth ES. Sildenafil for the treatment of pulmonary hypertension in pediatric patients. *Pediatr Cardiol*. 2009;30(7):871–82. Epub 2009 Aug 25.
12. Krishnan U, Krishnan S, Gewitz M. Treatment of pulmonary hypertension in children with chronic lung disease with newer oral therapies. *Pediatr Cardiol*. 2008;29(6):1082–6. Epub 2008 Jul 2.
13. MacKnight B, Martinez EA, Simon BA. Anesthetic management of patients with pulmonary hypertension. *Semin Cardiothorac Vasc Anesth*. 2008;12(2):91–6.
14. Galante D. Intraoperative management of pulmonary arterial hypertension in infants and children. *Curr Opin Anaesthesiol*. 2009;22(3):378–82.
15. Rosenzweig EB, Barst RJ. Pulmonary arterial hypertension in children: a medical update. *Indian J Pediatr*. 2009;76(1):77–81. Epub 2009 Apr 18.
16. Friesen RH, Williams GD. Anesthetic management of children with pulmonary arterial hypertension. *Paediatr Anaesth*. 2008;18(3):208–16.
17. Taylor K, Holtby H. Emergency interventional lung assist for pulmonary hypertension. *Anesth Analg*. 2009;109(2):382–5.
18. Ayers J, Graves SA. Perioperative management of total parenteral nutrition, glucose containing solutions, and intraoperative glucose monitoring in paediatric patients: a survey of clinical practice. *Paediatr Anaesth*. 2001;11(1):41–4.
19. Fösel TH, Uth M, Wilhelm W, Grüness V. Comparison of two solutions with different glucose concentrations for infusion therapy during laparotomies in infants. *Infusionsther Transfusionsmed*. 1996;23(2):80–4.
20. Gauda EB, McLemore GL, Tolosa J, Marston-Nelson J, Kwak D. Maturation of peripheral arterial chemoreceptors in relation to neonatal apnoea. *Semin Neonatol*. 2004;9(3):181–94.
21. Choudhry DK. Single-lung ventilation in pediatric anesthesia. *Anesthesiol Clin N Am*. 2005;23:693–708.
22. Rowe R, Andropoulos D, Heard M, et al. Anesthetic management of pediatric patients undergoing thoracoscopy. *J Cardiothorac Vasc Anesth*. 1994;8:563–6.
23. Kubota H, Kubota Y, Toyoda Y, et al. Selective blind endobronchial intubation in children and adults. *Anesthesiology*. 1987;67:587–9.

24. Rehman M, Sherlekar S, Schwartz R, et al. One lung anesthesia for video assisted thoracoscopic lung biopsy in a paediatric patient. *Paediatr Anaesth*. 1999;9:85–7.
25. Hammer GB, Harrison TK, Vricella LA, Black MD, Krane EJ. Single lung ventilation in children using a new paediatric bronchial blocker. *Paediatr Anaesth*. 2002;12(1):69–72.
26. Takahashi M, Yamada M, Honda I, Kato M, Yamamuro M, Hashimoto Y. Selective lobar – bronchial blocking for pediatric video-assisted thoracic surgery. *Anesthesiology*. 2001;94(1):170–2.
27. Chengod S, Chandrasekharan AP, Manoj P. Selective left bronchial intubation and left-lung isolation in infants and toddlers: analysis of a new technique. *J Cardiothorac Vasc Anesth*. 2005;19(5):636–41.
28. Gayes JM. Pro: one-lung ventilation is best accomplished with the Univent endotracheal tube. *J Cardiothorac Vasc Anesth*. 1993;7:103–7.
29. Kamaya H, Krishna PR. New endotracheal tube (univent tube) for selective blockade of one lung. *Anesthesiology*. 1985;63:342–3.
30. Hammer GB, Brodsky JB, Redpath JH, Cannon WB. The Univent tube for single-lung ventilation in paediatric patients. *Paediatr Anaesth*. 1998;8(1):55–7.
31. Arndt GA, DeLessio ST, Kranner PW, Orzepowski W, Ceranski B, Valtysson B. One-lung ventilation when intubation is difficult – presentation of a new endobronchial blocker. *Acta Anaesthesiol Scand*. 1999;43(3):356–8.
32. Yun ES, Saulys A, Popic PM, Arndt GA. Single-lung ventilation in a pediatric patient using a pediatric fibreoptically-directed wire-guided endobronchial blocker. *Can J Anaesth*. 2002;49(3):256–61.
33. Li PY, Gu HH, Liang WM. Sequential one-lung ventilation using one Arndt endobronchial blocker in a pediatric patient undergoing bilateral, video-assisted thoracoscopic surgery (VATS). *J Clin Anesth*. 2009;21(6):464.
34. Hammer GB, Fitzmaurice BG, Brodsky JB. Methods for single-lung ventilation in pediatric patients. *Anesth Analg*. 1999;89:1426–9.
35. Klein U, Karzai W, Bloos F, Wohlfarth M, Gottschall R, Fritz H, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia: a prospective study. *Anesthesiology*. 1998;88(2):346–50.
36. Fitzmaurice BG, Brodsky JB. Airway rupture from double-lumen tubes. *J Cardiothorac Vasc Anesth*. 1999;13:322–9.
37. Tezel C, Okur E, Baysungur V. Iatrogenic tracheal rupture during intubation with a double-lumen tube. *Thorac Cardiovasc Surg*. 2010;58(1):54–6.
38. Nicolai T. Pediatric bronchoscopy. *Pediatr Pulmonol*. 2001;31(2):150–64.
39. Slonim AD, Ognibene FP. Amnestic agents in pediatric bronchoscopy. *Chest*. 1999;116(6):1802–8.
40. Berkenbosch JW, Graff GR, Stark JM, Ner Z, Tobias JD. Use of a remifentanil-propofol mixture for pediatric flexible fiberoptic bronchoscopy sedation. *Paediatr Anaesth*. 2004;14(11):941–6.
41. Larsen R, Galloway D, Wadera S, Kjar D, Hardy D, Mirkes C, Wick L, Pohl JF. Safety of propofol sedation for pediatric outpatient procedures. *Clin Pediatr (Phila)*. 2009;48(8):819–23. Epub 2009 May 29.
42. Tobias JD. Sedation and anesthesia for pediatric bronchoscopy. *Curr Opin Pediatr*. 1997;9(3):198–206.
43. Dilos BM. Anesthesia for pediatric airway endoscopy and upper gastrointestinal endoscopy. *Int Anesthesiol Clin*. 2009;47:55–62.
44. Seybold JL. The use of dexmedetomidine during laryngoscopy, bronchoscopy, and tracheal extubation following tracheal reconstruction. *Pediatr Anesth*. 2007;17:1212–4.
45. Niggemann B, Haack M, Machotta A. How to enter the pediatric airway for bronchoscopy. *Pediatr Int*. 2004;46(2):117–21.
46. Zestos MM, Bhattacharya D, Rajan S, Kemper S, Haupert M. Propofol decreases waste anesthetic gas exposure during pediatric bronchoscopy. *Laryngoscope*. 2004;114(2):212–5.
47. Nussbaum E, Zagnoev M. Pediatric fiberoptic bronchoscopy with a laryngeal mask airway. *Chest*. 2001;120(2):614–6.
48. Bandla HP, Smith DE, Kiernan MP. Laryngeal mask airway facilitated fibreoptic bronchoscopy in infants. *Can J Anaesth*. 1997;44(12):1242–7.
49. Naguib ML, Streetman DS, Clifton S, Nasr SZ. Use of laryngeal mask airway in flexible bronchoscopy in infants and children. *Pediatr Pulmonol*. 2005;39(1):56–63.
50. Somri M, Barna Teszler C, Tome R, Kugelman A, Vaida S, Gaitini L. Flexible fiberoptic bronchoscopy through the laryngeal mask airway in a small, premature neonate. *Am J Otolaryngol*. 2005;26(4):268–71.
51. Picard E, Schwartz S, Goldberg S, Glick T, Villa Y, Kerem E. A prospective study of fever and bacteremia after flexible fiberoptic bronchoscopy in children. *Chest*. 2000;117(2):573–7.
52. Picard E, Goldberg S, Virgilis D, Schwartz S, Raveh D, Kerem E. A single dose of dexamethasone to prevent postbronchoscopy fever in children: a randomized placebo-controlled trial. *Chest*. 2007;131(1):201–5.
53. Nussbaum E. Pediatric fiberoptic bronchoscopy: clinical experience with 2,836 bronchoscopies. *Pediatr Crit Care Med*. 2002;3(2):171–6.
54. Salva PS, Theroux C, Schwartz D. Safety of endobronchial biopsy in 170 children with chronic respiratory symptoms. *Thorax*. 2003;58(12):1058–60.
55. Shah R, Reddy AS, Dhende NP. Video assisted thoracic surgery in children. *J Minim Access Surg*. 2007;3(4):161–7.
56. Oak SN, Parelkar SV, Satishkumar KV, Pathak R, Ramesh BH, Sudhir S, et al. Review of video-assisted thoracoscopy in children. *J Minim Access Surg*. 2009;5(3):57–62.
57. de Campos JR, Andrade Filho LO, Werebe EC, Minamoto H, Quim AO, Filomeno LT, et al. Thoracoscopy in children and adolescents. *Chest*. 1997;111(2):494–7.
58. Tobias JD. Thoracic surgery in children. *Curr Opin Anaesthesiol*. 2001;14(1):77–85.
59. Sundararajan L, Parikh DH. Evolving experience with video-assisted thoracic surgery in congenital cystic lung lesions in a British pediatric center. *J Pediatr Surg*. 2007;42(7):1243–50.
60. Dutta S, Mihailovic A, Benson L, Kantor PF, Fitzgerald PG, Walton JM, Langer JC, Cameron BH. Thoracoscopic ligation versus coil occlusion for patent ductus arteriosus: a matched cohort study of outcomes and cost. *Surg Endosc*. 2008;22(7):1643–8. Epub 2007 Nov 20.
61. Byington CL, Spencer LY, Johnson TA, Pavia AT, Allen D, Mason EO, Kaplan S, Carroll KC, Daly JA, Christenson JC, Samore MH. An epidemiological investigation of a sustained high rate of pediatric parapneumonic empyema: risk factors and microbiological associations. *Clin Infect Dis*. 2002;34(4):434–40. Epub 2002 Jan 3.
62. Aziz A, Healey JM, Qureshi F, Kane TD, Kurland G, Green M, et al. Comparative analysis of chest tube thoracostomy and video-assisted thoracoscopic surgery in empyema and parapneumonic

- effusion associated with pneumonia in children. *Surg Infect (Larchmt)*. 2008;9(3):317–23.
63. Chen CY, Chen JS, Huang LM, Lee PI, Lu CY, Lee YC, et al. Favorable outcome of parapneumonic empyema in children managed by primary video-assisted thoracoscopic debridement. *J Formos Med Assoc*. 2003;102(12):845–50.
64. Kang DW, Campos JR, Andrade Filho Lde O, Engel FC, Xavier AM, Macedo M, et al. Thoracoscopy in the treatment of pleural empyema in pediatric patients. *J Bras Pneumol*. 2008;34(4):205–11.
65. Chen JS, Huang KC, Chen YC, Hsu HH, Kuo SW, Huang PM, Lee JM, Lee YC. Pediatric empyema: outcome analysis of thoracoscopic management. *J Thorac Cardiovasc Surg*. 2009;137(5):1195–9. Epub 2009 Feb 7.
66. Cohen G, Hjortdal V, Ricci M, Jaffe A, Wallis C, Dinwiddie R, Elliott MJ, de Leval MR. Primary thoracoscopic treatment of empyema in children. *J Thorac Cardiovasc Surg*. 2003;125(1):79–83; discussion 83–4.
67. Gates RL, Caniano DA, Hayes JR, Arca MJ. Does VATS provide optimal treatment of empyema in children? A systematic review. *J Pediatr Surg*. 2004;39(3):381–6.
68. Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. *Pediatrics*. 2005;115(6):1652–9.
69. St Peter SD, Tsao K, Spilde TL, Keckler SJ, Harrison C, Jackson MA, et al. Thoracoscopic decortication vs. tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. *J Pediatr Surg*. 2009;44(1):106–11.
70. Ho AC, Chen CY, Yang MW, Liu HP. Use of the Arndt wire-guided endobronchial blocker to facilitate one-lung ventilation for pediatric empyema during video-assisted thoracoscopy. *Chang Gung Med J*. 2005;28(2):104–10.
71. Tobias JD. Variations on one-lung ventilation. *J Clin Anesth*. 2001;13(1):35–9.
72. Ho AC, Chung HS, Lu PP, Hong CL, Yang MW, Liu HP. Facilitation of alternative one-lung and two-lung ventilation by use of an endotracheal tube exchanger for pediatric empyema during video-assisted thoracoscopy. *Surg Endosc*. 2004;18(12):1752–6. Epub 2004 Oct 13.
73. Nezafati MH, Soltani G, Vedadian A. Video-assisted ductal closure with new modifications: minimally invasive, maximally effective, 1,300 cases. *Ann Thorac Surg*. 2007;84(4):1343–8.
74. Mavroudis C. Forty-six years of patient ductus arteriosus division at Children's Memorial Hospital of Chicago. Standards for comparison. *Ann Surg*. 1994;220(3):402–10.
75. Wang JK, Hwang JJ, Chiang FT, Wu MH, Lin MT, Lee WL, Lue HC. A strategic approach to transcatheter closure of patent ductus: gianturco coils for small-to-moderate ductus and Amplatzer duct occluder for large ductus. *Int J Cardiol*. 2006;106(1):10–5. Epub 2005 Sep 15.
76. Daher AH. Infective endocarditis in neonates. *Clin Pediatr (Phila)*. 1995;34(4):198–206.
77. Vanamo K. Video-assisted thoracoscopic versus open surgery for persistent ductus arteriosus. *J Pediatr Surg*. 2006;41(7):1226–9.
78. Villa E. Video-assisted thoracoscopic clipping of patent ductus arteriosus: close to the gold standard and minimally invasive competitor of percutaneous techniques. *J Cardiovasc Med (Hagerstown)*. 2006;7(3):210–5.
79. Villa E. Paediatric video-assisted thoracoscopic clipping of patent ductus arteriosus: experience in more than 700 cases. *Eur J Cardiothorac Surg*. 2004;25(3):387–93.
80. Burke RP. Video-assisted thoracoscopic surgery for patent ductus arteriosus in low birth weight neonates and infants. *Pediatrics*. 1999;104(2 Pt 1):227–30.
81. Muralidhar KS, Shetty DP. Ventilation strategy for video-assisted thoracoscopic clipping of patent ductus arteriosus in children. *Paediatr Anaesth*. 2001;11(1):45–8.
82. Miyagi K. One-lung ventilation for video-assisted thoracoscopic interruption of patent ductus arteriosus. *Surg Today*. 2004;34(12):1006–9.
83. Odegard KC. Intraoperative recurrent laryngeal nerve monitoring during video-assisted thoracoscopic surgery for patent ductus arteriosus. *J Cardiothorac Vasc Anesth*. 2000;14(5):562–4.
84. Clark DC. Esophageal atresia and tracheoesophageal fistula. *Am Fam Physician*. 1999;59(4):910–6; 919–20.
85. Keckler SJ, St Peter SD, Valusek PA, Tsao K, Snyder CL, Holcomb GW 3rd, Ostlie DJ. VACTERL anomalies in patients with esophageal atresia: an updated delineation of the spectrum and review of the literature. *Pediatr Surg Int*. 2007;23(4):309–13. Epub 2007 Feb 15.
86. Geneviève D, de Pontual L, Amiel J, Sarnacki S, Lyonnet S. An overview of isolated and syndromic oesophageal atresia. *Clin Genet*. 2007;71(5):392–9.
87. Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.
88. Gross RE. The surgery of infancy and childhood. WB Saunders: Philadelphia; 1953.
89. Okamoto T, Takamizawa S, Arai H, Bitoh Y, Nakao M, Yokoi A, Nishijima E. Esophageal atresia: prognostic classification revisited. *Surgery*. 2009;145(6):675–81. Epub 2009 Apr 11.
90. Aziz D, Chait P, Kreichman F, Langer JC. Image-guided percutaneous gastrostomy in neonates with esophageal atresia. *J Pediatr Surg*. 2004;39(11):1648–50.
91. Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Paediatr Anaesth*. 2005;15(7):541–6.
92. Lugo B, Malhotra A, Guner Y, Nguyen T, Ford H, Nguyen NX. Thoracoscopic versus open repair of tracheoesophageal fistula and esophageal atresia. *J Laparoendosc Adv Surg Tech A*. 2008;18(5):753–6.
93. Orford J. Advances in the treatment of oesophageal atresia over three decades: the 1970s and the 1990s. *Pediatr Surg Int*. 2004;20(6):402–7. Epub 2004 May 18.
94. Narang S, Harte BH, Body SC. Anesthesia for patients with a mediastinal mass. *Anesthesiol Clin N Am*. 2001;19:559–79.
95. Takeda SI, Miyoshi S, Akashi A, Ohta M, Minami M, Okumura M, et al. Clinical spectrum of primary mediastinal tumors: a comparison of adult and pediatric populations at a single Japanese institution. *J Surg Oncol*. 2003;83:24–30.
96. Davis RD, Oldham NH, Sabiston DC. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management and results. *Ann Thorac Surg*. 1987;44:229–37.
97. Sairanen H, Leijala M, Louhimo I. Primary mediastinal tumors in children. *Eur J Cardiothorac Surg*. 1987;1:148–51.
98. Azarow KS, Pearl RH, Zurcher R, Edwards FH, Cohen AJ. Primary mediastinal masses: a comparison of adult and pediatric populations. *J Thorac Cardiovasc Surg*. 1993;106:67–72.
99. Shamberger RC, Holzman RS, Griscom NT, Tarbell NJ, Weinstein HJ. CT quantification of tracheal cross sectional area as a guide to the surgical and anesthetic management of children with anterior mediastinal mass. *J Pediatr Surg*. 1991;26:138–42.

100. Sakakeeny-Zaal K. Pediatric orthopnea and total airway obstruction. *Am J Nurs.* 2007;107:40–3.
101. Slinger P, Karsli C. Management of the patient with a large anterior mediastinal mass: recurring myths (Editorial). *Curr Opin Anaesthesiol.* 2007;20:1–3.
102. Hack HA, Wright NB, Wynn RF. The anaesthetic management of children with anterior mediastinal masses. *Anaesthesia.* 2008;63(8):837–46.
103. Bechard P, Letourneau L, Lacasse Y, Cote D, Bussieres JS. Perioperative cardiorespiratory complications in adults with mediastinal mass: incidence and risk factors. *Anesthesiology.* 2004;100:826–34.
104. Victory RA, Casey W, Doherty P, Breatnach F. Cardiac and respiratory complications of mediastinal lymphomas. *Anaesth Intens Care.* 1993;21:366–9.
105. Sanborn PA, Michna E, Zurokowski D, Burrows PE, Fontaine PJ, Connor L, et al. Adverse cardiovascular and respiratory events during sedation of pediatric patients for imaging examinations. *Radiology.* 2005;237:288–94.
106. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology.* 1990;73:826–30.
107. Anghelescu DL, Burgoyne LL, Liu T, Li CS, Pui CH, Hudson MM, et al. Clinical and diagnostic imaging findings predict anesthetic complications in children presenting with malignant mediastinal masses. *Paediatr Anaesth.* 2007;17:1090–8.
108. Rice TW, Rodriguez RM, Light RW. The superior vena cava syndrome: clinical characteristics and evolving etiology. *Medicine.* 2006;85:37–42.
109. Arya LS, Narain S, Tomar S, Thavaraj V, Dawar R, Bhargawa M. Superior vena cava syndrome. *Indian J Pediatr.* 2002;69:293–7.
110. Lam JCM, Chui CH, Jacobsen AS, Tan AM, Joseph VT. When is a mediastinal mass critical in a child? An analysis of 29 children. *Pediatr Surg Int.* 2004;20:180–4.
111. Azizkhan RG, Dudgeon DL, Buck JR, Colombani PM, Yaster M, Nichols D, et al. Life-threatening airway obstruction as a complication to the management of mediastinal masses in children. *J Pediatr Surg.* 1985;20(6):816–22.
112. Chaignaud BE, Bonsack TA, Kozakewich HP, Shamberger RC. Pleural effusions in lymphoblastic lymphoma: a diagnostic alternative. *J Pediatr Surg.* 1998;33:1355–7.
113. Das DK. Serous effusions in malignant lymphomas: a review. *Diagn Cytopathol.* 2006;3:335–47.
114. Güllüo lu MG, Kılıçaslan Z, Toker A, Kayalci G, Yilmazbayan D. The diagnostic value of image guided percutaneous fine needle aspiration biopsy in equivocal mediastinal masses. *Langenbecks Arch Surg.* 2006;39:222–7.
115. Chait P, Rico L, Amaral J, Connolly B, John P, Temple M. Ultrasound-guided core biopsy of mediastinal masses in children. *Pediatr Radiol.* 2005;35:S76.
116. Lachar W, Shahab I, Saad A. Accuracy and cost-effectiveness of core needle biopsy in the evaluation of suspected lymphoma: a study of 101 cases. *Arch Pathol Lab Med.* 2007;131:1033–9.
117. Annessi V, Paci M, Ferrari G, Sgarbi G. Ultrasonically guided biopsy of mediastinal masses. *Interact Cardiovasc Thorac Surg.* 2003;2:319–21.
118. Gupta A, Kumar A, Walters S, Chait P, Irwin MS, Gerstle JT. Analysis of needle versus open biopsy for the diagnosis of advanced stage pediatric neuroblastoma. *Pediatr Blood Cancer.* 2006;47:875–9.
119. Borenstein SH, Gerstle T, Malkin D, Thorner P, Filler RM. The effects of prebiopsy corticosteroid treatment on the diagnosis of mediastinal lymphoma. *J Pediatr Surg.* 2000;35:973–6.
120. Rampello E, Fricia T, Malaguarnera M. The management of tumor lysis syndrome. *Nat Clin Pract Oncol.* 2006;3:438–47.
121. Neuman GG, Weingarten AE, Abramowitz RM, Kushins LG, Abramson AL, Ladner W. The anesthetic management of a patient with an anterior mediastinal mass. *Anesthesiology.* 1984;60:144–7.
122. Torchio R, Gulotta C, Perbondi A, Ciacco C, Guglielmo M, Orlandi F, et al. Orthopnea and tidal expiratory flow limitation in patients with euthyroid goiter. *Chest.* 2003;124:133–40.
123. Hnatiuk OW, Corcoran PC, Sierra P. Spirometry in surgery for anterior mediastinal masses. *Chest.* 2001;120:1152–6.
124. Vander Els NJ, Sorhage F, Bach AM, Straus DJ, White DA. Abnormal flow volume loops in patients with intrathoracic Hodgkin's disease. *Chest.* 2000;117:1256–61.
125. Frawley G, Low J, Brown TCK. Anaesthesia for an anterior mediastinal mass with ketamine and midazolam infusion. *Anaesth Intens Care.* 1995;23:610–2.
126. Bergman NA. Reduction in resting end-expiratory position of the respiratory system with induction of anesthesia and neuromuscular paralysis. *Anesthesiology.* 1982;57:14–7.
127. Lin SH, Su NY, Hsue SS, Ting CK, Yien HW, Cheng HC, et al. Anesthetic management of patients with giant mediastinal tumors – a report of two cases. *Acta Anaesthesiol Sin.* 1999;37:133–9.
128. Riley RH, Raper GD, Newman MAJ. Helium-oxygen and cardiopulmonary bypass standby in anesthesia for tracheal stenosis. *Anaesth Intens Care.* 1994;22:710–3.
129. Asai T. Emergency cardiopulmonary bypass in a patient with a mediastinal mass. *Anaesthesia.* 2007;62:859–60.
130. Takeda S, Miyoshi S, Omori K, Okumura M, Matsuda H. Surgical rescue for life-threatening hypoxemia caused by a mediastinal tumor. *Ann Thorac Surg.* 1999;68:2324–6.
131. Langham Jr MR, Kays DW, Ledbetter DJ, Frentzen B, Sanford LL, Richards DS. Congenital diaphragmatic hernia. Epidemiology and outcome. *Clin Perinatol.* 1996;23(4):671–88.
132. Deeprest J. Current consequences of prenatal diagnosis of congenital diaphragmatic hernia. *J Pediatr Surg.* 2006;41(2):423–30.
133. Suita S et al. Fetal stabilization for antenatally diagnosed diaphragmatic hernia. *J Pediatr Surg.* 1999;34(11):1652–7.
134. Bosenberg AT, Brown RA. Management of congenital diaphragmatic hernia. *Curr Opin Anaesthesiol.* 2008;21(3):323–31.
135. Bohn D. Congenital diaphragmatic hernia. *Am J Respir Crit Care Med.* 2002;166:911–5.
136. Vitali SH, Arnold JH. Bench-to-bedside review: ventilator strategies to reduce lung injury – lessons from pediatric and neonatal intensive care. *Crit Care.* 2005;9(2):177–83. Epub 2004 Nov 4.
137. Wung JT. Congenital diaphragmatic hernia: survival treated with very delayed surgery, spontaneous respiration, and no chest tube. *J Pediatr Surg.* 1995;Vo1301(No 3):406–9.
138. Boloker J. Congenital diaphragmatic hernia in 120 infants treated consecutively with permissive hypercapnea/spontaneous respiration/elective repair. *J Pediatr Surg.* 2002;37:357–66.
139. Kays DW. Detrimental effects of standard medical therapy in congenital diaphragmatic hernia. *Ann Surg.* 1999;230(3):340–51.
140. Bryner BS et al. Congenital diaphragmatic hernia requiring extracorporeal membrane oxygenation: does timing of repair matter? *J Pediatr Surg.* 2009;44(6):1165–71.

141. Guner YS et al. Outcome analysis of neonates with congenital diaphragmatic hernia treated with venovenous vs. venoarterial extracorporeal membrane oxygenation. *J Pediatr Surg.* 2009; 44(9):1691–701.
142. van den Hout L. Can we improve outcome of congenital diaphragmatic hernia? *Pediatr Surg Int.* 2009;25:733–43.
143. Colvin J et al. Outcomes of congenital diaphragmatic hernia: a population-based study in Western Australia. *Pediatrics.* 2005;116(3):e365–3.
144. Liem NT, Dien TM, Ung NQ. Thoracoscopic repair in the neonatal intensive care unit for congenital diaphragmatic hernia during high-frequency oscillatory ventilation. *J Laparoendosc Adv Surg Tech A.* 2010;20(1):111–4.
145. Hsu HT et al. Total intravenous anesthesia for repair of congenital diaphragmatic hernia: a case report. *Kaohsiung J Med Sci.* 2004;20(9):465–9.
146. Liem NT. Thoracoscopic surgery for congenital diaphragmatic hernia: a report of nine cases. *Asian J Surg.* 2003;26(4):210–2.
147. Nguyen TL, Le AD. Thoracoscopic repair for congenital diaphragmatic hernia: lessons from 45 cases. *J Pediatr Surg.* 2006;41(10):1713–5.
148. Hussain HK et al. Imaging-guided core biopsy for the diagnosis of malignant tumors in pediatric patients. *AJR Am J Roentgenol.* 2001;176(1):43–7.
149. Elston WJ et al. Safety of research bronchoscopy, biopsy and bronchoalveolar lavage in asthma. *Eur Respir J.* 2004;24(3): 375–7.
150. Lex C et al. Airway eosinophilia in children with severe asthma: predictive values of noninvasive tests. *Am J Respir Crit Care Med.* 2006;174(12):1286–91.
151. Regamey N et al. Quality, size, and composition of pediatric endobronchial biopsies in cystic fibrosis. *Chest.* 2007;131(6): 1710–7.
152. Molina-Teran A et al. Safety of endobronchial biopsy in children with cystic fibrosis. *Pediatr Pulmonol.* 2006;41(11):1021–4.
153. Bishop MK, Mallory GB, White FV. Pediatric lung transplantation: perspectives for the pathologist. *Pediatr Dev Pathol.* 2008;11(2):85–105.
154. Mahmoud M et al. Dexmedetomidine and ketamine for large anterior mediastinal mass biopsy. *Paediatr Anaesth.* 2008;18(10):1011–3.
155. Cahill AM et al. CT-guided percutaneous lung biopsy in children. *J Vasc Interv Radiol.* 2004;15(9):955–60.
156. Gluer S et al. Thoracoscopic biopsy in children with diffuse parenchymal lung disease. *Pediatr Pulmonol.* 2008;43(10): 992–6.
157. Shah PL, Hansell D, Lawson PR, Reid KBM, Morgan C. Pulmonary alveolar proteinosis: clinical aspects and current concepts on pathogenesis. *Thorax.* 2000;55:67–771.
158. Trapnell BC, Whitsett JA, Nakata K. Mechanisms of disease: pulmonary alveolar proteinosis. *N Engl J Med.* 2003;349: 2527–39.
159. Lippmann M, Mok MS, Wasserman K. Anaesthetic management for children with alveolar proteinosis using extracorporeal circulation. Report of two cases. *Br J Anaesth.* 1977;49:173–7.
160. Mahut B, de Blic J, Le Bourgeois M, Beringer A, Chevalier JY, Scheinmann P. Partial and massive lung lavages in an infant with severe pulmonary alveolar proteinosis. *Pediatr Pulmonol.* 1992;13:50–3.
161. Moazam F, Schmidt JH, Chesrown SE, Graves SA, Sauder RA, Drummond J, et al. Total lung lavage for pulmonary alveolar proteinosis in an infant without the use of cardiopulmonary bypass. *J Pediatr Surg.* 1985;20:398–401.
162. Paschen C, Reiter K, Stanzel F, Teschler H, Gries M. Therapeutic lung lavages in children and adults. *Respir Res.* 2005; 6:138.
163. Paquet C, Karsli C. Technique of lung isolation for whole lung lavage in a child with pulmonary alveolar proteinosis. *Anesthesiology.* 2009;110:190–2.
164. Bliss D, Silen M. Pediatric thoracic trauma. *Crit Care Med.* 2002;30(11 Suppl):S409–15.
165. Holmes JF, Sokolove PE, Brant WE, Kuppermann N. A clinical decision rule for identifying children with thoracic injuries after blunt torso trauma. *Ann Emerg Med.* 2002;39(5):492–9.
166. Peclet MH et al. Thoracic trauma in children: an indicator of increased mortality. *J Pediatr Surg.* 1990;25(9):961–5.
167. Bonadio WA, Hellmich T. Post-traumatic pulmonary contusion in children. *Ann Emerg Med.* 1989;18(10):1050–2.
168. Karamakar MK, Ho A. Acute pain management of patients with multiple fractured ribs. *J Trauma.* 2003;54:615–25.
169. Cadzow SP, Armstrong KL. Rib fractures in infants: red alert. *J Paediatr Child Health.* 2000;36:322–6.
170. Bulloch B et al. Cause and clinical characteristics of rib fractures in infants. *Pediatrics.* 2000;105(4):E48.
171. Roux P, Fisher RM. Chest injuries in children: an analysis of 100 cases of blunt chest trauma from motor vehicle accidents. *J Pediatr Surg.* 1992;27(5):551–5.
172. Haxhija EQ, Nöres H, Schober P, Höllwarth ME. Lung contusion-lacerations after blunt thoracic trauma in children. *Pediatr Surg Int.* 2004;20(6):412–4. Epub 2004 Apr 30.
173. Taira BR et al. Ventilator-associated pneumonia in pediatric trauma patients. *Pediatr Crit Care Med.* 2009;10(4):491–4.
174. Cullen ML. Pulmonary and respiratory complications of pediatric trauma. *Respir Care Clin N Am.* 2001;7(1):59–77.
175. Hancock BJ, Wiseman NE. Tracheobronchial injuries in children. *J Pediatr Surg.* 1991;26(11):1316–9.
176. Grant WJ, Meyers RL, Jaffe RL, Johnson DG. Tracheobronchial injuries after blunt chest trauma in children – hidden pathology. *J Pediatr Surg.* 1998;33(11):1707–11.
177. Eichelberger MR, Randolph JG. Thoracic trauma in children. *Surg Clin N Am.* 1981;61(5):1181–97.
178. Toronto Lung Transplant Program, Hospital for Sick Children Statistics 2009 (personal communication).
179. Golianu B, Hammer GB. Pain management for pediatric thoracic surgery. *Curr Opin Anaesthesiol.* 2005;18:13–21.
180. Nunn JF, Slavin G. Posterior intercostal nerve blocks for pain relief after cholecystectomy. Anatomical basis and efficacy. *Br J Anaesth.* 1980;52:253–60.
181. Gibson MP, Vetter T, Crow JP. Use of continuous retropleural bupivacaine in postoperative pain management for pediatric thoracotomy. *J Pediatr Surg.* 1999;34(1):199–201.
182. Krane EJ, Dalens BJ, Murat I, Murrell D. The safety of epidurals placed during general anesthesia. *Reg Anesth Pain Med.* 1998;23:433–8.
183. Tsui BC, Seal R, Koller J, Entwistle L, Haugen R, Kearney R. Thoracic epidural analgesia via the caudal approach in pediatric patients undergoing fundoplication using nerve stimulation guidance. *Anesth Analg.* 2001;93(5):1152–5.

184. Tsui BC. Innovative approaches to neuraxial blockade in children: the introduction of epidural nerve root stimulation and ultrasound guidance for epidural catheter placement. *Pain Res Manag.* 2006;11(3):173–80.
185. Ingelmo P et al. The optimum initial pediatric epidural bolus: a comparison of four local anesthetic solutions. *Paediatr Anaesth.* 2007;17(12):1166–75.
186. Goodarzi M. Comparison of epidural morphine, hydromorphone and fentanyl for postoperative pain control in children undergoing orthopaedic surgery. *Paediatr Anaesth.* 1999;9(5): 419–22.
187. Serlin S. Single-dose caudal epidural morphine in children: safe, effective, and easy. *J Clin Anesth.* 1991;3(5): 386–90.

40

Anesthetic Management of Thoracic Trauma

Stephen V. Panaro

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Key Points

- The initial assessment and stabilization of the thoracic trauma patient is critical for successful outcomes. An understanding of the relevant anatomy and familiarization with the signs and symptoms of injury to the vital structures will minimize the chance of missed injury which could be catastrophic.
- Airway management and lung isolation provide challenges to the anesthesiologist. Identification of the location of a tracheobronchial injury preoperatively will dictate the method of isolation beyond the injury. Lung isolation techniques are more challenging to novice anesthesiologists. Anesthesiologists who may be asked to manage thoracic trauma patients should familiarize themselves with these techniques.
- There is no level I evidence for the management of pulmonary contusion. There are similarities between the contused lung and ARDS and the patients who present with pulmonary contusion should be ventilated with lung protective strategies.
- Management of cardiac trauma requires an understanding of the type of injury and prompt diagnosis is of paramount importance. Signs of cardiac tamponade must be identified quickly and the pericardium decompressed urgently. Echocardiography is a useful tool in evaluating injury and guiding therapy in unstable patients if available.
- Injury to the thoracic aorta is increasingly being managed with endovascular techniques, but not all patients

are candidates. An understanding of the physiology of the thoracic aortic clamp and its implications for hemodynamic management remains important. Similarly, strategies for spinal cord protection during open repair must be considered. Expectant management of minimal aortic injury may become more common.

- Anesthesiologists play an integral role in the management of pain in the patients with chest wall injury. There is potential for improved outcomes with epidural analgesia, but many patients will not be candidates for neuraxial analgesia. In the patients who will meet exclusion criteria, other techniques including paravertebral blocks should be considered.

Introduction

Thoracic trauma is a morbid business. The American College of Surgeons estimates it is associated with a 10% mortality [1] with 16,000 deaths annually representing 25% of all trauma deaths. Considering that injury is the leading cause of death from ages 1 to 45 (more than half of all deaths ages 13–32 and 80% in teenage years) [2] and the leading cause of years of life lost before 75, its impact is enormous [3]. Since the vital structures in the chest are so well protected by the bony thorax, a great deal of force is required to disrupt them, and they are uncommonly injured in isolation in blunt trauma.

Indeed, in 70% of cases, insults to the chest are associated with multisystem injury.

This chapter will attempt to describe thoracic trauma in terms of the underlying injury and its treatment. This approach is not new and dates (at least) to the ancient Egyptian Edwin Smith Papyrus in the seventeenth century BC. While our tools and management have changed (we no longer treat hemorrhage with the binding of fresh meat on the first day), the organization of the chapter will follow theirs – structured to some degree by injury type.

While the presentation of a patient with traumatic injury to the thorax can seem daunting, the principles in managing these patients are the familiar backbone of our specialty. A rational stepwise approach to the evaluation and management of these patients will not only yield the best results, but also make it clear that there is nothing mystical about them. That process begins, as always, with an understanding of the relevant physiology, anatomy and the tools we use to assess them.

Relevant Anatomy

The chest is, by definition, the upper part of the trunk between the neck and the abdomen formed by the 12 thoracic vertebrae and the corresponding ribs. Thoracic trauma may include injury to the chest wall, pleura, airways, heart, great vessels, diaphragm and esophagus. The implications of injury vary by structure and its mechanism of insult. The most lethal injuries are those involving the mediastinal structures. The mediastinum itself is divided into four parts (see Chap. 14, Fig. 14.1). The anterior mediastinum lies between the sternum and the pericardium and contains little other than fat, lymph nodes, the internal thoracic (mammary) vessels and the thymus. The middle mediastinum contains the pericardium, heart, lower half of the superior vena cava, ascending aorta, tracheal bifurcation as well as the pulmonary arteries and veins. The posterior mediastinum is the space between the tracheal bifurcation and vertebral column and contains the descending aorta, azygous, esophagus and thoracic duct. Lastly, the superior mediastinum is bound by the manubrium and the first four vertebrae. It holds the aortic arch, brachiocephalic veins, upper half of the SVC the left common carotid and subclavian arteries as well as the brachiocephalic trunk. Stab injuries to the heart are through the classic precordium (so-called “box of death”) bound by the sternal notch superiorly, nipples laterally and inferiorly by the anterior ribs in 80% of the cases. On the other hand, gunshot injuries to the heart enter through the precordium in a minority of patients (46%) suggesting that a bullet would anywhere on the torso should raise concern of injury to the heart.

The Lethal Six

Many thoracic injuries are highly lethal. In fact, only two-thirds of the patients will actually reach the hospital alive. Of those that do, the immediate identification and treatment of

the six most lethal injuries is paramount, and the assessment of the thoracic trauma patient should follow the protocol detailed in ATLS®. The six most immediately lethal injuries to the chest that are sought include airway obstruction, tension pneumothorax, cardiac tamponade, open pneumothorax, massive hemothorax and flail chest.

The diagnosis of airway obstruction should be clear to any anesthesiologist. The physical findings of apnea, cyanosis, stridor, subcutaneous emphysema and the appearance of a patient with air hunger should be familiar to us. The etiology may be from avulsed teeth, secretions, expanding neck hematomas, laryngeal trauma, tracheal tears or even tracheal transection. As always, immediate intubation is indicated in any patient with airway compromise. Special considerations for patients with airway disruption will be discussed later in the chapter as will the management of the airway in the trauma patient.

Tension pneumothorax occurs when air enters the pleural space and cannot exit. This results in a shift of the mediastinum, kinking of the superior and inferior vena cava and a profound decrease in cardiac output. Patients present with respiratory distress, unilateral breath sounds, neck vein distension, tracheal deviation (rarely) and cyanosis (very late finding). If this constellation of symptoms occurs just after intubation, one must become immediately suspicious. An old surgical adage holds that one should never have a chest X-ray (CXR) of a tension pneumothorax. This constellation of findings should be immediately treated with needle decompression (14 gauge catheter in the second intercostal space, midclavicular line – classically) followed by tube thoracostomy.

Cardiac Tamponade is most often the result of penetrating trauma, but can be seen in blunt trauma. The pericardial sac is tough and fibrous and when fluid builds quickly, only 75–100 ccs will cause tamponade physiology. The classic Beck's triad (JVD, hypotension and muffled heart sounds) are only present in one-third of the patients. While Kussmaul's sign (rise in central venous pressure with inspiration) is reliable, it is not practical in the trauma setting since few patients have a central line in place before the diagnosis must be made. The equalization of pressures (should one happen to have a Swan-Ganz catheter in place they might find an equalization of diastolic pressures including right atrial, right ventricular, pulmonary artery and even pulmonary artery occlusion pressure) or systolic to diastolic gradient of less than 30 mmHg may also suggest tamponade. Most commonly in trauma, the diagnosis will be suggested by ongoing hypotension without obvious blood loss. FAST (Focused Assessment with Sonography for Trauma) examination is highly accurate [4]. The patient can be temporized with pericardiocentesis occasionally, but this procedure is technically less challenging in the patient with chronic pericardial effusions than in traumatic tamponade because of the small amount of fluid necessary to cause the physiology and because clotted blood can be difficult to aspirate. In reality, trauma patients in extremis should be treated with ED thoracotomy. Those more stable should be evaluated with FAST, TEE if the expertise is available or

even a subxiphoid pericardial window depending on local experience, resources and clinical scenario. The latter can be performed in the operating room, but can be considered in the emergency department if necessary [5]. Once the diagnosis is made, the patient should be treated aggressively with fluids until they can be taken for definitive treatment. If a penetrating injury to the myocardium has occurred, it may be possible to treat without cardiopulmonary bypass [6]. This is fortuitous, because the administration of large volumes of heparin is often contraindicated in the trauma patient. Adenosine may provide the surgeon with 15 or 20 s of asystole and has been described to facilitate repair [7].

The other three of the lethal six are usually not difficult to diagnose. Massive hemothorax (>1,500 cc of blood or more than 200 cc/h for 4 h) should be suspected in any trauma patient with shock and absent or distant breath sounds on one side. A CXR will show the fluid in the chest but should not be necessary in all cases. This is an indication for thoracotomy. Most cases of more moderate hemothorax can be treated with tube thoracostomy and appropriate resuscitation. The last two of the six (open pneumothorax and flail chest) should be easily recognizable. We will discuss the treatment of the latter in the section on analgesia for trauma patients.

Traumatic Airway Management

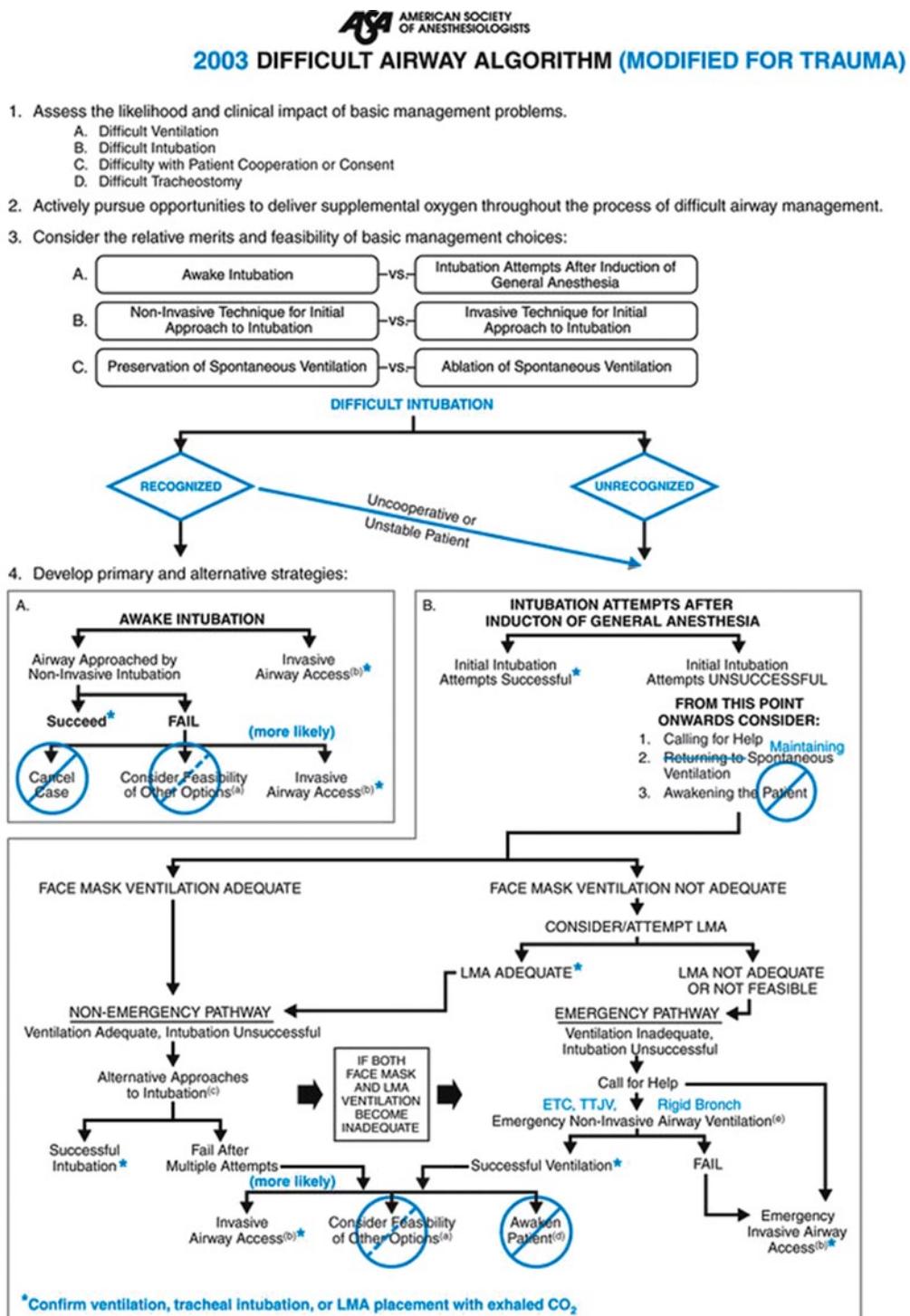
Few topics seem to generate more discussion among anesthesiologists than the presentation of a trauma patient in need of an emergent airway. There are questions of whether manual inline stabilization is always helpful or can be harmful in restricting the view at laryngoscopy [8, 9]. There are questions of whether Sellick and his 26 patients should have had the influence they have over the last half century [10–13], and there are a myriad of devices to aid us. The discussion is not without merit, since the consequences of failure are dire. The fact that 2% of blunt trauma patients have a cervical spine injury adds to the angst. Furthermore, every method of airway intervention causes motion of the cervical spine including a jaw thrust and placement of an LMA. The basic tenants of airway management remain in place, however, and the ASA difficult airway algorithm (modified for trauma) remains a valuable tool [14] (Fig. 40.1). The modifications for trauma recognizes, among other things, that stopping and returning another day is not feasible and that a surgical airway may often be the best first option. As such, anesthesiologists who treat trauma patients should be familiar with the techniques and equipment necessary for percutaneous or open cricothyrotomy or tracheostomy. An outstanding recent review of the literature on the topic of airway management in the trauma patient (beyond the scope of this chapter) also provides a perspective [15]. What should never be lost amid all the controversy is that the cornerstone of emergent airway management remains direct laryngoscopy. There are strong historical data suggesting that direct laryngoscopy is both highly successful

and associated with few credible reports of neurologic deterioration even in the face of known cervical spine injury [15, 16]. A recent review at a major trauma center, in fact, looked at over 6,000 patients who were intubated within 1 h of their arrival. Only 31 required a surgical airway and 87% of these survived their hospitalization. Of the four patients that died, none were judged to be airway related. This study did not include the number of patients that were intubated fiberoptically. Their high success rate compared to other series may have been a result of an attending anesthesiologist's presence as part of their protocol. While their protocol calls for inline stabilization and cricoid pressure, they wisely will relax one or both of these if there is a sense that intubation is being hampered by either technique [17].

This is not to minimize the role of awake (or asleep) fiberoptic intubation in patients with a difficult airway or known or suspected cervical spine injury. This is by far the author's preference for known difficult airways in stable cooperative patients with cervical spine injuries. No technology has yet replaced it. Still, the reality is that awake fiberoptic intubation requires a cooperative patient and can be difficult with blood in the airway. Many of the limitations to fiberoptic intubation can be overcome, however, with the use of an adult bronchoscope with a powerful external light source. Anesthesiologists most often use smaller bronchoscopes for use in double lumen endobronchial tubes. The use of an adult bronchoscope adds stiffness which aids in directing the bronchoscope. An external light source adds far greater illumination, and the larger port on an adult sized bronchoscope can be used to either suction or blow oxygen to free the view of secretions or blood. Lastly, a 7.0 endotracheal tube fits snugly around this bronchoscope minimizing the chance the tube will catch on the arytenoids or epiglottis after the scope has passed into the trachea. Still, it is always best to be familiar with the other emergency airway devices available in one's practice such as the bougie, light wand, Glidescope®, Airtraq®, McGrath® video laryngoscope or kits for retrograde intubation. This is especially true since awake, cooperative patients are in the minority in the trauma population. In one 7-year review, in fact, 83% of the patients were legally intoxicated on presentation [16].

Lung Isolation

One of the more challenging aspects of the management of patients with thoracic injury is lung isolation which may be required for injury to the thorax. Techniques include right mainstem intubation, Univent® tubes, a variety of commercially available bronchial blockers and right- and left-sided double lumen tubes. Since right mainstem intubation will most often result in ventilation of only the right middle and lower lobes, it would be expected to result in the highest shunt fraction and higher rates of hypoxia. Each of the other devices requires some expertise, however, and they each have an equivalent high failure rate of 39% in faculty with limited



- a. Other options include (but are not limited to): surgery utilizing face mask or LMA anesthesia, local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway. **Judgment required. Rarely appropriate for trauma patients.**
- b. Invasive airway access includes surgical or percutaneous tracheostomy or cricothyrotomy.
- c. Alternative non-invasive approaches to difficult intubation include (but are not limited to): use of different laryngoscope blades, **LMA** as an intubation

- conduit (with or without fiberoptic guidance), fiberoptic intubation (FOB), intubation stylet or tube changer (airway exchange catheter, AEC) light wand, retrograde intubation, and blind oral or nasal intubation.
- d. Consider re-preparation of the patient for awake intubation or canceling surgery. **Rarely applicable in the trauma patient.**
- e. Options for emergency non-invasive airway ventilation include (but are not limited to): rigid bronchoscope (**Rigid Bronch**), esophageal-tracheal combitube ventilation (ETC), or transtracheal jet ventilation (TTJV).
- f. **Extubation strategies include: evaluation of the airway with FOB and extubation over an airway exchange catheter (AEC).**

FIG. 40.1. ASA difficult airway algorithm (modified for trauma) (difficult airway algorithm (modified for trauma) [2005] is reprinted with permission from the American Society of Anesthesiologists).

thoracic experience of less than two cases per month [18]. In this study all malpositions were corrected easily by more experienced thoracic staff. The choice of isolation technique must be based on other factors. Traditionally, double lumen tubes (DLTs) are the standard of performance for lung isolation. In experienced hands, isolation can be achieved quickly and definitively in most cases. In institutions with extensive experience, in fact, right-sided tubes can be used with as few complications (desaturation, high peak airway pressures, etc.) as left-sided tubes [19]. Still, there may be disadvantages to DLTs especially in the trauma population. They may be associated with more airway trauma (especially if an airway injury already exists) with placement. Further, if the patient is to remain intubated following the procedure, double lumen endobronchial tubes should be changed to single lumen endotracheal tubes for many reasons. Most obviously, pulmonary toilet is much more difficult with standard length suction devices in the ICU. Their bulk may lead to torsion and injury to the airway over the long term in a patient who is awake and moving. They also have a much larger outer diameter and higher work of breathing given their added length. Recently, three commercially available bronchial blockers have been shown to perform well when compared to left-sided DLTs in their ability to isolate the lung. They did require a longer time to place and had to be repositioned frequently, however [20]. They may be a better option for thoracic trauma patients, although anesthesiologists' familiarity should also play a role in selecting a lung isolation device.

Tracheobronchial Injury

Like so many injuries to the thorax, tracheobronchial injuries are highly lethal. In an older autopsy series of trauma patients, 81% of the patients with tracheobronchial rupture died before reaching a hospital [21]. In a more recent review of a single institution's 15-year experience including over 12,000 trauma patients 0.85% of the patients reaching the hospital had a tracheobronchial injury (TBI). The numbers were very different for blunt and penetrating mechanisms (0.4% incidence for blunt trauma victims, 4.5% for penetrating) [22]. This review considered all traumatic airway injuries including those of the upper airway and thoracic trachea. In the larger of the North American series, around 60% of these injuries treated will be the result of penetrating trauma [23]. These patients tend to have better outcomes, possibly because of fewer associated injuries [22, 23]. Patients who do appear after a delay in diagnosis often will present when granulation tissue appears in their airway causing a narrowing and postobstructive pneumonia or recurrent pneumothoraces.

Clinical Signs

There are classic signs of TBI, but they can be misleading or absent, and a high index of suspicion is required. Surprisingly,

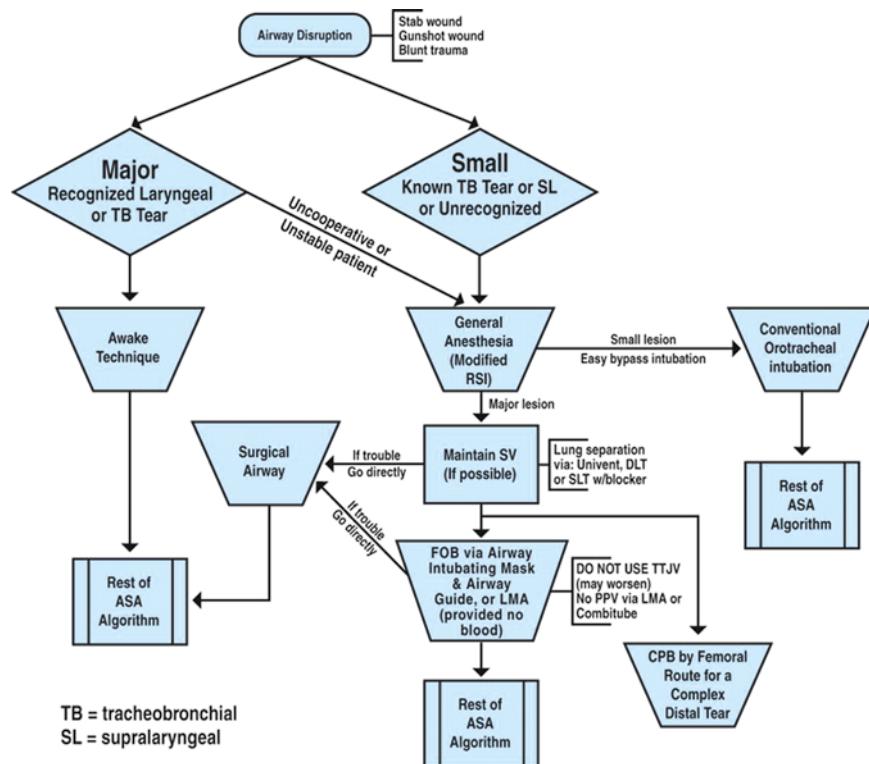
in a comprehensive review of all TBIs reported in the literature up until 1996, the median time to diagnosis was 9 days [24]. More recently in a single institution review, long delays in diagnosis were not reported [22, 23]. When present the classic signs of subcutaneous or mediastinal emphysema, hemoptysis, pneumothorax (especially with a large air leak or with a failure to expand the lung after tube thoracostomy), tension pneumothorax as well as unexplained dyspnea should all raise suspicion of an airway injury. Blunt TBIs may be associated with fractures of the first rib, clavicle, sternum, chest wall and lung contusions. The location of injury to the tracheobronchial tree has been consistent over several series [14, 23, 24]. By far, most injuries seem to be within 2 cm of the carina with a predilection for the right side. The latter may be a result of a heavier right lung with a shorter right mainstem bronchus in deceleration injuries. The most likely theory explaining the consistent data showing injury close to the bifurcation is that a rapid deceleration of relatively mobile lungs in the pleura against a fixed carina causes a tear. Bronchial rupture may also be from compression of the chest against a closed glottis. This has been shown in a canine model.

Airway Management and Lung Isolation in TBI

Whatever the mechanism, securing the airway in patients with TBIs can be a daunting task. Indeed, some very heroic measures have been described including thoractomy [25], jet ventilation via intrabronchial catheters [26] and ECMO [27]. The ASA does have an airway disruption algorithm which emphasizes maintaining spontaneous ventilation whenever possible [14] (Fig. 40.2). The critical tool for both assessing the injury as well as controlling the airway is fiberoptic bronchoscopy. The goal in most cases should be to place the cuff of the endotracheal tube beyond the injury or at least to protect the injury from positive pressure ventilation in some fashion. This is complicated by the fact that most blunt injuries to the trachea are within 2 cm of the carina [14, 23, 24]. In this instance, placement of a side-specific double lumen endotracheal tube is often most appropriate, although caution must be exercised in placing these bulky rigid tubes past an already injured airway. Passing the cuff of a single lumen tube beyond the injury and using a bronchial blocker for lung isolation in more proximal injuries seems prudent. This also has the added advantage of avoiding the changing of the endotracheal tube at the end of the procedure should the patient need to remain intubated. A scenario of cross field ventilation can also be envisioned but should be rare. In every case knowledge of the location of injury is paramount in providing the best airway.

One cannot overemphasize the importance of maintaining spontaneous ventilation in patients with severe tracheal injury. There have been reports of patients arriving with transected or nearly transected airways who maintain spontaneous ventilation through a "neo-trachea" via mediasternal tissues. Attempts at blind instrumentation can be disastrous [28]. Unfortunately making the diagnosis can be difficult prior to

FIG. 40.2. ASA airway disruption algorithm emphasizing spontaneous ventilation and the avoidance of positive pressure ventilation above injury whenever possible (airway disruption algorithm [2005] is reprinted with permission from the American Society of Anesthesiologists).



the need for intubation although clues may be present in a lateral c-spine film. Suspicion should be heightened in a patient with difficulty in breathing and any of the classic signs of TBI including subcutaneous emphysema. Fortunately complete transaction of the airways in patients surviving to reach the hospital is quite rare. The liberal use of bronchoscopy should help lower the incidence of missed injury, help define injury when present and help secure the airway [23]. In the Toronto series, 29% of patients with TBI required interventions more complex than direct laryngoscopy. These included around 10% each of FOB, surgical airway and temporary airway through the wound [22].

There is literature evolving for conservative management of tracheobronchial injuries. Most have focused on iatrogenic injury to the membranous portion of the trachea. Unfortunately these injuries are becoming more common and represented half of the injuries in a recent series [29]. They may be as common as 1 in 20,000 intubations or 0.12% of DLT placements [30]. Patients may present removed from the trauma with either a delay in their diagnosis or a delay in their treatment. These patients allow for surgical planning, controlled airway management and have a lower mortality [24].

Aortic Injury

In 1958 Parmley reviewed 296 cases of aortic injury from the Armed Forces Institute of Pathology and found an 80% mortality prior to arrival at a hospital [31]. It is unlikely that we

have made much progress on that front in the intervening five decades [32]. Since this is thought to be largely a deceleration injury, it may be that restraints have had little impact. We have, however, made progress on the patients who do reach the hospital and may be seeing a major advancement over the last few years as thoracic stent grafts become increasingly common.

Because most aortic injuries occur following a rapid deceleration and are most often at the isthmus, traditional discussions of the pathophysiology of the tear have focused on the interaction between the fixed descending aorta and relatively mobile heart and great vessels. Still, injuries have been described in the ascending aorta, more distal thoracic aorta and abdominal aorta suggesting that other mechanisms may play a role as well. Other mechanisms described include a pinching of the aorta against the vertebral column and a “water hammer effect” describing a sudden occlusion of the aorta and increase in aortic pressure. These have recently been summarized elsewhere [33].

Diagnosis

The prompt diagnosis of this injury is essential. As is often quoted, 30–50% of the patients who reach the hospital will die within the first 24 h [31, 34]. Imaging is crucial since there can be few external signs of aortic injury. While the classic findings on CXR such as widening of the mediastinum, blurring of the aortic knob, deviation of the NG tube and shift of the right bronchus all suggest the diagnosis, they are not diagnostic.

Helical computed tomography has become the dominant modality for this purpose. It is fast, allows the quick evaluation of concomitant injuries elsewhere in the body, and has a sensitivity approaching 100% [35]. Transesophageal echocardiography (TEE), MRI and intravascular ultrasound have also all been described, although it is unclear if any are as accurate as helical CT. TEE, for example, can often not visualize the aortic arch as well.

The treatment of aortic injury once a diagnosis is made is almost always prompt. It should be noted for completeness that there is a small subgroup of patients presenting with hemodynamic stability that have been treated expectantly with tight blood pressure and heart rate control either because their severe comorbid conditions precluded operative repair or because their injury was considered minimal [36, 37]. Although small in number, these patients have done quite well. Still, defining minimal aortic injury is an ongoing process and most patients will present to the operating room. A period of nonoperative management may be indicated for patients who are unstable from associated injuries, those with traumatic brain injury, severe pulmonary contusion unable to tolerate one lung ventilation, etc. While surgery may be successfully delayed while associated injuries are evaluated and stabilized with the use of beta blockers and antihypertensive agents, the care of these complex patients will eventually fall to the anesthesiologist.

Despite our advances, a prospective look at 50 trauma centers in North America over a two and a half year period suggested an overall mortality of 31% [34]. All patients who arrived in extremis or who ruptured prior to definitive therapy died. Mortality in patients who were operated on was 14% with an 8.7% paraplegia rate. This study was published before endovascular grafts were increasing in use, and all patients who were operated on had an open repair.

Open Repair and Spinal Cord Protection

Open surgical repair in general begins with a high left posterolateral thoracotomy and some form of lung isolation, most typically a double lumen endobronchial tube (DLT). Hypoxia may be a formidable challenge in patients with associated pulmonary contusion. The pros and cons of various methods of lung isolation were reviewed earlier in the chapter. The anesthesiologist must be prepared for the massive hemodynamic swings that accompany proximal thoracic aortic cross clamping (sometimes above the left subclavian artery) as well as attending to all the issues of blood loss and the comorbidities the patient brings to the operating theater. There are three main methods of surgical repair all aimed at preserving spinal cord function. The first is speed in a traditional clamp and sew technique. The advantage of this technique is its simplicity and avoidance of the large doses of systemic heparin used for cardiopulmonary bypass. Bypass from the left atrium (or pulmonary vein) to the distal aorta involves the use of a relatively simple centrifugal pump system and also minimizes the use of

heparin. Bypass from the femoral vein cannulation site to the femoral artery requires an oxygenator in the circuit and may require high-dose anticoagulation, although heparin-coated tubing may minimize the dose [33]. There may be advantages in having an oxygenator in the circuit, however, if the patient has lung injury where one lung ventilation may not be optimal [33]. Clearly it would seem that any technique that limits the need for anticoagulation in the multi-injured trauma patient is advantageous, although concerns of short-term anticoagulation may be exaggerated in patients without head injury [34]. The pros and cons of these techniques are beyond the scope of this text, but the anesthesiologist must be familiar with the norms of the institution and be prepared to manage the techniques preferred by their surgeons. Although lumbar cerebrospinal fluid (CSF) drainage has not been proven in blunt aortic injury, its use was shown prospectively to be of benefit in patients undergoing thoracic aortic aneurysm repair and should be considered in the stable, cooperative patient [38]. Even under the best circumstances, open repair can negatively affect the patient's underlying pulmonary, cardiac and neurologic status [39].

Endovascular Repair

Recently, attention has focused on endovascular treatment of thoracic aortic injuries. There are many theoretical advantages of this approach. For patients with closed head injury, it can be done without significant heparinization, large hemodynamic swings complicating the management of intracranial hypertension and can even be done in reverse Trendelenburg if needed. It can be done in patients in traction for long bone injuries, does not require lung isolation and avoids position changes for patients with pelvic injury than may exacerbate pelvic hematoma. These facts broaden the patient population who can be treated and avoids delays in treating others. Published series show improved mortality, fewer perioperative complications compared to open repair and a low or zero rate of paraplegia [39–42]. The low rate of paraplegia may relate to the short segment of thoracic aorta that needs coverage in the typical injury [39]. Concerns remain, however. Many are technical and some revolve around the specifics of a device developed for aneurysmal disease being placed in a normal, smaller thoracic aorta. There can also be difficulties with the proximity to the left subclavian artery, and there can be challenges in dealing with the curvature of the aorta. Still, there has been a dramatic shift away from open repair to endovascular treatments. Open repair has fallen from 100% of repairs in 1997 to 35% in the second American Association for the Surgery of Trauma study in 2008 [43, 44]. These numbers of course reflect the behavior of 18 select trauma centers. The percentage of stent grafts placed in the country as a whole is probably smaller. Still, in these two studies there has been a dramatic fall in procedure-related mortality and paraplegia (8.7 to 1.6% overall from first study to the second). Device issues (early endoleak, left subclavian artery compromise,

left carotid artery occlusion (resulting in CVA), etc.) remain a concern. There also remains a lack of long-term follow up of these devices, and how they will perform as a young trauma patient ages is as yet unknown. These patients will also need long term, perhaps lifelong follow up to assure endoleaks do not develop. Lastly, it is unclear if some of these devices were placed in patients who had minimal aortic injury and may not have required treatment at all as pointed out in the discussion that accompanies this paper [42].

Pulmonary Contusion

Physiology

Pulmonary contusion is a clinical entity that complicates as many as 65% of blunt chest trauma patients who present for surgery [45]. In a sobering look at the long-term sequela, a recent review suggested that 70% of patients will have deficits in pulmonary function 6 months after injury and will report a loss of physical function [46]. Signs on presentation are as one would expect namely tachypnea, hypoxia, hypercarbia, wheezing and sometimes hemoptysis. CXR and even CT findings can lag behind the clinical picture by hours. Chest ultrasound may aid in the rapid diagnosis especially as the extended focused assessment with ultrasonography for trauma (EFAST) evolves [47, 48]. The gross pathology results from the loss of vessel integrity at the alveolar capillary membrane leading to intraparenchymal and alveolar hemorrhage and edema. Surfactant production decreases and shunt ensues. As in ARDS the lung becomes functionally smaller as alveoli fill with blood and edema. Pain then leads to splinting and progressive atelectasis. Worse, pulmonary contusion can lead to true ARDS. Evidence continues to mount that lung injury is itself inflammatory, and the localized inflammatory response may be what leads to ARDS [49–52]. Further, the immediate inflammatory response in the lung may lead to delayed immune suppression that increases patients' susceptibility to an infectious challenge later [53, 54]. Despite its inflammatory nature, steroids cannot be recommended [55].

Intraoperative Management

Making specific, evidence-based recommendations based on the available literature is difficult. This is underscored by the absence of a single level I evidence-based recommendation in the EAST (Eastern Association for the Surgery of Trauma) guidelines for pulmonary contusion [55]. Level II recommendations describe supportive care such as optimal pain management (with epidurals when possible), avoiding obligatory ventilation and overly aggressive resuscitation. The anesthesiologists' primary role in lung contusion outside the operating room will be to assist in the management of pain. This will be discussed in more detail later. In the operating theater, issues will center around fluid and ventilatory management. Adapting lung protective strategies developed for and accepted in

ARDS patients seems prudent. Because alveolar over distension and alveolar opening and collapse can only exacerbate the inflammatory process, part of this should be recruitment maneuvers and PEEP [55, 56]. The initial resuscitation should not be compromised, but the administration of fluids afterwards should be meticulous in an effort not to augment extravascular lung water. The best method for monitoring fluid management is open to question although dynamic assessments to predict fluid responsiveness (improvement in cardiac output) seem to be better than static measurements of CVP and PCWP in a myriad of recent clinical trials. There is also a suggestion that Hextend® may have a role, but the utility of starch based volume expanders is recently coming under more scrutiny [57].

Blunt Cardiac Injury

Pathophysiology

The term blunt cardiac injury (BCI) covers a wide range of injuries whose clinical significance is related to both the type and severity of the injury. The pathophysiology results from either direct transfer of energy during the impact of the thorax, the rapid deceleration of the heart, as a result of the impact of the right ventricle against the sternum or compression of the heart between the sternum and spine [58]. The pattern and pathophysiology of injury will reflect the details of the impact and position of the heart in the cardiac cycle. The ventricles for example are most vulnerable at end diastole and the valves most vulnerable when closed. Even modest impacts can lead to sudden cardiac death, most commonly from ventricular arrhythmias. Commotio cordis, for example, results from an impact during the vulnerable moment of repolarization just prior to T wave peak [59, 60]. Most deaths due to blunt cardiac injury require more force, however. Almost every injury one can imagine can occur and has been described. The heart can be contused, torn or ruptured (freely or septal). Coronary arteries can be torn or become thrombosed. The pericardium can become distended with blood and cause tamponade. Finally, the heart is a muscle, and can be contused like any other. When it is, local hemorrhage, edema and often necrosis cause poor performance. As the contused portion begins to swell, perfusion to that portion of myocardium may be compromised causing ventricular dysfunction to be exacerbated. Further, this may make the patient susceptible to arrhythmias possibly from a reentry mechanism [61]. Of concern, these arrhythmias can present very late (up to 6 days in one case report) after an initial 24 h arrhythmia free period [62]. Lastly, the practitioner must remember that myocardial performance may be drastically compromised even without direct injury to the heart. This is most commonly and sometimes dramatically seen in patients with traumatic brain injury. The most common mechanism of cardiac injury remains motor vehicle crashes in the most recent series. In patients who died of blunt trauma, 66% had either a cardiac or thoracic aortic injury (or both). Injuries to the right atrium and to the right ventricle predominate [63].

The approach to the patient is determined by their clinical presentation. Taking a history from the patient who is able to provide one will give valuable clues not only by detailing symptoms, but also by documenting prior cardiac issues that may help avoid confusion of acute and chronic conditions. The physical exam should focus not only on the heart, but also on associated chest wall injuries that will raise the index of suspicion for associated BCI. These include chest tenderness, crepitus, seatbelt marks, etc. Beck's triad of hypotension, muffled heart sounds and distended neck veins or pulses paradoxus suggest tamponade and urgent surgical attention.

Echocardiography has become an incredibly useful tool in the assessment of the BCI patient, and this begins with the FAST (Focused Assessment with Sonography for Trauma) assessment. FAST has proven extremely reliable in the assessment of the pericardium and can be completed in less than a minute and a half with a sensitivity as high as 100% [64, 65] for patients with suspected pericardial tamponade. Formal echocardiography (transthoracic or transesophageal when transthoracic is inadequate) is the primary tool for assessing hemodynamic instability in patients with BCI. Hemodynamic instability can result from etiologies that require very different treatments, and defining whether failure is due to acute valvular insufficiency, septal rupture leading to left to right shunt, cardiac rupture, wall motion abnormalities from contusion, LAD thrombosis from crush injury or any other pathology is essential. Despite its usefulness as a tool in the sickest patients, it is not a cost-effective screening tool. The EAST practice guidelines echo most authors' opinion and the bulk of the literature when they state that formal echocardiography adds little to the hemodynamically stable patient and should be reserved for patients with instability or with a clinical question that cannot be explained [66, 67]. Part of the rationale for this statement is that even in patients diagnosed with BCI by echocardiography, in hemodynamically stable patients there was no sequela of the injury that required treatment even at 1 year follow up [68]. One of the difficulties in BCI, in fact, is evaluating and triaging patients with significant chest trauma and risk for BCI (e.g., patients with fractured ribs, sternum and pulmonary contusion) who have no initial symptoms of BCI. The negative predictive value of two serial negative troponin I tests and a normal ECG was 100% in one study suggesting that these patients need no further observation or treatment [69]. While an abnormal ECG does correlate with the risk of developing a complication requiring treatment in BCI [70], the findings are often nonspecific and may not help define the pathology or physiology that is crucial to aiding in treatment.

Management

Specific generalizations for the anesthesiologists managing the patient with blunt cardiac injury are few since the individual patient's injury pattern and physiology must dictate specific treatments. As we have stated, defining any abnormality of the function of the ventricle is generally accomplished with echocardiography. Clinical suspicion of the possibility of

tamponade and an understanding of the signs will aid in the prompt diagnosis of this problem. In truth, all three signs of Beck's triad may not be present in trauma patients with tamponade who are profoundly hypovolemic. The most common etiology is rupture of the right atrial appendage followed by rupture of the right ventricle [63, 70, 71]. This is true in autopsy and clinical series although the percentage of right-sided rupture is higher in clinical series presumably because of the high lethality of left ventricular rupture. Pericardiocentesis is used less frequently than in the past because of a higher number of complications and lower sensitivity/specificity compared to FAST. For unstable patients either subxiphoid window or anterolateral thoracotomy is preferred as discussed in the section on pericardial tamponade.

Cardiac failure can occur from several different etiologies in blunt trauma. As stated above, contusions can cause inflammation, hemorrhage within the myocardium and cellular necrosis all of which change the compliance of the ventricle and its contractility. Complicating this may be small vessel thrombosis worsening ischemia [72]. Coronary artery occlusion, laceration and thrombosis have all been described as well [71, 72]. Acute valvular incompetence may also precipitate failure. Care is supportive and consists of appropriate fluid resuscitation based on the injury and the use of vasopressors and inotropes. There are case reports of intra-aortic balloon counter pulsation (IABP). Since most cardiac contusion involves the right ventricle, avoiding common causes for increased pulmonary vascular resistance (e.g., hypoxia, hypercarbia) would be prudent. When pulmonary contusion is present, the increased afterload may worsen right ventricular function. Increasing mean intrathoracic pressures further with large tidal volumes should be avoided. While vasopressors may be unavoidable, vasopressin specifically may improve systemic hemodynamics without increasing pulmonary vascular resistance, although this is hardly proven [73]. While heightened vigilance for arrhythmias seems prudent, no prophylactic treatment is warranted and management is as dictated by ACLS. Arrhythmias are the most common finding in patients with BCI. If one includes sinus tachycardia and bradycardia in the definition, they are present in the majority of patients [71]. Arrhythmias requiring treatment, conversely, will be rare. In a large meta-analysis, only around 2% of patients out of over 2200 in their population suffered arrhythmias requiring treatment and some of these were frequent PVCs that may no longer be considered worthy of pharmacologic intervention [70].

Pain Management for Blunt Thoracic Trauma

Modalities

The rationale for optimal pain control for the population with blunt thoracic injury is not complex and lies in the high rate of morbidity and mortality in these patients and the now accepted tenants of its treatment. Rib fractures are present

in roughly 10% of trauma admissions and they are a marker of more severe injuries [74]. Ninety percent of patients will have associated injuries and 12% will die of their injuries [74]. More pertinently, 35% will have a pulmonary complication [74]. Flail chest in isolation carries a 16% mortality [75]. 30% of patients with seven or more rib fractures will die [75]. Elderly patients may be particularly vulnerable with a 36% rate of pulmonary complications and an 8% mortality for isolated rib fractures reported [76]. A combination of age and number of ribs fractured dramatically increased morbidity and mortality with each additional rib fracture in patients over 65 causing a 27% increased risk of pneumonia and a 19% increase in the risk of death [77]. The management of blunt thoracic trauma has evolved from stabilization of the bony injury (either physical or “pneumatic” via positive pressure ventilation) to a reliance on pain control and adequate chest physiotherapy [78]. There seems to be little debate about this strategy in the current literature. What is less obvious is how to provide optimal pain management. The ideal regimen would provide long lasting analgesia and allow the patient to comfortably participate in chest physiotherapy. It would improve dynamic measurements of respiratory function. It would be easy to administer, have a favorable side effect profile and be cost effective. We have no such technique or pharmaceutic. What we do have is a variety of tools that can each be useful in a given circumstance. Each has pros and cons and they should be viewed as complementary in many cases. As clinicians, we often feel one technique is superior to another. Free of bias, we can see that many of these modalities have their uses and can and should be used in combination depending on the clinical picture. Until the perfect solution is created, we must recognize that while some of our tools are more valuable than others, many of them will be needed in busy trauma centers to optimize patient management. We will review the modalities, their strengths and weakness and the relevant literature.

Systemic narcotics remain the most prevalent modality for pain management in patients with blunt chest trauma. They have the advantage of ease of administration when taken either orally, via intermittent intravenous injection, continuous intravenous infusion or by patient controlled analgesia pumps. There are no procedural related complications and they are inexpensive. They improve visual analog scales and may improve vital capacity [79]. When compared to epidural analgesia, however, patients retain more CO_2 , have a lower PaO_2 and do not improve maximum inspiratory pressure. They also cause respiratory depression, suppress cough and increase sedation [79].

Intrapleural anesthesia involves infiltration of local anesthetic into the pleural space either via an indwelling thoracostomy tube or placement of a dedicated intrapleural catheter [80, 81]. The procedure is a unilateral modality that has few hemodynamic penalties. The theoretical and real disadvantages are considerable, however. Instillation of local anesthetic through a chest tube requires its clamping to retain the drug in the intrapleural space risking tension pneumothorax [78].

Hemothorax may impair absorption across the pleura [82]. Concerns have also been raised about high plasma levels from intrapleural infusions of local anesthetic. Phrenic nerve paralysis and Horner's syndrome have been described [83–85]. Furthermore, a complication of placement of an intrapleural catheter in a patient without thoracostomy tube is pneumothorax. Position of the catheter in relation to the fractured ribs, the number and location of the fractured ribs and patient position may all affect the technique's efficacy. When compared in a randomized fashion (albeit in small numbers) to epidural analgesia, the intrapleural catheter provided less pain relief, and more narcotic use. Epidural analgesia also improved negative inspiratory pressure and tidal volume. The authors concluded that continuous epidural block was superior to intrapleural block [81]. Although some have used the technique with success, an admittedly small study more recently showed no benefit compared even to systemic narcotics [82, 86]. In the end, the large number of variables that affect this technique, the short duration of effect, the lack of consistent data showing efficacy and the potential complications severely limit its use in our practice.

Intercostal nerve blocks have a long history of use and success in patients with blunt chest trauma [87]. They involve injections of the intercostal nerve proximal to the point of injury and at a level above and below the injured rib. While some authors advocate the block be performed proximal to the mid axillary line to ensure blockade of the lateral and anterior cutaneous branches of the intercostal nerve, this should only be necessary when analgesia of the skin is required [87, 88]. The block will be unilateral and should have few hemodynamic consequences. Intercostal nerve block has been shown to improve peak expiratory flow rate as well as arterial oxygen and carbon dioxide tensions, but these effects last only hours [89–91]. Despite this, Shanti observed that the vast majority of trauma patients need only one or two injections [92]. The blocks are not sedating. Still there are limitations to the technique. Palpating fractured ribs can be painful, and there can be technical difficulties with the block in higher ribs because of the scapula. Of more concern is that the rate of pneumothorax is 1.4% for each individual intercostals nerve blocked leading to an overall rate of 8.7% per patient in Shanti's study [92]. With patients who have several ribs fractured, there would be a need for multiple injections raising the risk not only of pneumothorax but of local anesthetic toxicity and increased pain of the procedure. Intercostal catheters have been described in small numbers, but the anatomic endpoint of placement can be nebulous and maintaining the proper position of the catheter a challenge [78, 93, 94]. In the end, intercostal blocks are simple to perform and can remain a viable alternative in patients who have contraindications or unsuccessful placement of either an epidural catheter or paravertebral block, especially in patients who have a tube thoracostomy in place.

Paravertebral blocks using both a single shot and continuous infusion of local anesthetic are gaining momentum.

This seems to be true both in the thoracic trauma and the thoracic surgery literature. Although expertise in the technique may be more limited than it is for epidural placement, the theoretical advantages may soon change that [95, 96]. There seems to be mounting enthusiasm for this technique first described over 100 years ago, and the discussion has begun on the possibility that it will replace epidural analgesia in the world of thoracic surgery and thoracic trauma [97, 98]. Because the technique involves the block of the intercostal nerve, its dorsal ramus and the sympathetic chain, it produces a dense sensory and sympathetic block [97]. Because the block is unilateral (although unintentional epidural injection is a potential complication), there is less hypotension when compared to epidural analgesia [98, 99]. The block is reported as being simple to perform and perhaps easier to place than a thoracic epidural, although trouble threading the catheter into the paravertebral space has been reported more than once [96, 100]. There are other advantages as well. When compared to epidural analgesia, there seems to be less urinary retention, and there are theoretic reasons to expect less respiratory depression and pruritis since there is no neuraxial opioids as they are commonly with an epidural. It also may be safer to place in patients who are sedated or even ventilated [78, 89]. Placement of a paravertebral block could in theory relax strict restrictions on the placement of epidural catheters in the face of mild coagulopathy or DVT prophylaxis with low molecular weight heparins. Further, many trials of epidurals in blunt thoracic trauma patients have used any injury to the spine as an exclusion criterion [101]. The presence of a spine fracture was in fact the most frequent exclusion criteria accounting for more than twice as many as any other in a frequently quoted study [101]. This may not necessarily exclude placement of a paravertebral catheter. It would, for example, be hard to imagine that a lumbar transverse process fracture would be a contraindication for a paravertebral block or catheter. There are also now being described ultrasound guided techniques of placement that may make this technique safer and easier [102–104]. Lastly, the paravertebral approach does seem to be effective. It has been shown to improve pain, bedside spirometry and blood gasses [100]. In one small study (15 patients, each arm) it was as effective as epidural analgesia. Unfortunately, these are the only patients comparing the techniques in trauma patients. If one were to extrapolate data from thoracotomy patients, paravertebral catheters still seem to do as well, but again the data are very limited and that extrapolation may or may not be valid [97].

Still some challenges remain for paravertebral blocks. The most obvious may be familiarity with the technique among current practitioners. Secondly, the technique is not complication free. In Karmakar's series of 15 patients having a continuous paravertebral catheter placed for unilateral rib fractures, for example, there was one inadvertent placement of the catheter in the epidural space that was not appreciated until a large volume of local anesthetic was given. That patient became hypotensive. Twenty percent of the patients in

that same series had bilateral analgesia. It is unclear whether that was from epidural spread or spread to the contralateral paravertebral space, but these facts taken together along with the known incidence of pneumothorax and pleural placement make the position of the catheter to be less than certain [100, 105]. The failure rate is also as high as 10% and vascular puncture is 3.8% [105]. Dural puncture and subarachnoid injection have also been described [106, 107]. One of the 15 patients that received a paravertebral infusion in Mohta's recent trial suffered a seizure presumably from local anesthetic toxicity [100]. Certainly strict attention to dose is necessary especially if bilateral catheters would be contemplated for patients with bilateral rib fractures

In the end, the application of paravertebral blocks in blunt trauma may gain wider acceptance as familiarity with the technique spreads. There are numerous theoretical advantages and some of these have been realized in small trials. Ultrasound guidance may add to the safety of the technique. While data in trauma patients remains limited for now, this technique will undoubtedly become more commonplace. Its utility at present is limited both by a lack of wide spread technical expertise and its greater utility in patients with unilateral rib fractures

Epidural analgesia remains the standard by which all other pain management modalities are compared. Its theoretical advantages are myriad. It provides nearly immediate bilateral pain relief. It is less sedating than systemic narcotics so patients can participate in pulmonary toilet [108]. It has been shown to increase functional residual capacity, vital capacity, tidal volume, compliance and decrease the movement of flail segments as well as to increase PO_2 [87, 109, 110]. There have been two randomized prospective trials comparing systemic narcotics and epidural analgesia [101, 109]. In the study by Bulger, there was an impressive decrease in the rate of nosocomial pneumonia and duration of mechanical ventilation [101]. In the Ullman study, there were fewer ventilator days, a shorter ICU stay and a shorter hospitalization. They also had fewer tracheostomies and a larger tidal volume [109]. These results were achieved without what the author would propose is the most effective manner to use an epidural suggesting that the technique could be even more effective. The Ullman study used only epidural narcotics, while the Bulger study had no standardization of their epidural regimen. Neither study used patient controlled epidural analgesia (PCEA) or programmed intermittent epidural bolus (PIEB) which should result in improved pain control in the trauma patient as it has in the obstetric patient [111, 112]. There is also evidence in the thoracic surgery literature that a combination of local anesthetic and opioids is more effective than either alone [113]. Epidurals may even modulate the immune response in thoracic trauma patients [114]. In the EAST pain management guidelines for blunt trauma there is a single level I statement for the clinical application of pain management modalities "Epidural analgesia is the optimal modality of pain relief for blunt chest wall injury and is the preferred technique after severe blunt thoracic trauma" [78].

Recommendations

Despite all of these data and 30 years of experience, there remains as stated above only two randomized controlled trials showing improved outcomes with epidural pain management compared to systemic narcotics, and both of these trials were very small (46 enrolled was the larger of the two). The size of the studies actually points to some of the concerns of epidural analgesia. In the Bulger study, for example, 408 patients were identified over three and a half years, and yet 282 met exclusion criteria and 80 could not be consented leaving only 46 [101]. By their own admission, they were fairly conservative in their enrollment (all patients with any spine fracture were excluded). The point remains that many patients who would benefit from epidural placement will not be able to receive one, even if the criteria for exclusion in that study were relaxed. For example, a patient with a lumbar transverse process fracture may be expected to have an epidural placed without significant additional risk [101]. Still other exclusion criteria will remain firm (hemodynamic instability, coagulopathy, altered mental status). Epidurals can cause hypotension especially in the hypovolemic patient or after large volume bolus with local anesthetic. Epidural infections have also been documented [108]. Epidural catheters can be challenging to place especially in patients in pain. Lastly, epidural combinations of local anesthetic and opioids can cause pruritis, nausea, urinary retention and respiratory depression.

The aim of pain management for the blunt thoracic trauma patient is twofold. First and most obviously pain control is an end onto itself. Patient satisfaction and comfort should be the anesthesiologist's goal under any circumstance. It is improving their respiratory mechanics through that pain relief that will alter outcome. If we can break the cycle of shallow breathing and poor cough leading to atelectasis, sputum retention, decreased functional residual capacity (FRC) and worsening hypoxia from V/Q mismatch, we can hopefully intubate fewer patients and avoid all the complications that come with it. These include the need for sedation, ventilator-associated pneumonia, DVT, the possibility of nutritional deficiency, etc. The elderly are particularly hard hit by this process as detailed before [77]. Epidural catheters and paravertebral blocks seem to offer the best pain control. Each has its strengths and weakness, and therapy must be individualized. A patient who is able to achieve a vital capacity of 12–15 cc/kg without significant sedation from systemic narcotics, for example, may require no invasive procedures. The presence of a protocol in each institution to standardize therapy may be helpful. It should be noted that the use of other systemic agents for the use of pain control have not been mentioned. Interestingly, there is a paucity of data for the use of NSAIDs or acetaminophen in thoracic injury. Still they are frequently used for the outpatient management of rib fractures, and as a tenant of multimodality therapy it is reasonable to include them in the management of patients without contraindication. Figure 40.3 represents a modified version of the protocol at our institution. It may serve as a model for departments wishing to address the issue

of optimum pain control for their hospital. Even with a protocol in place, the clinician must be aware that patients vary in their clinical presentation and analgesic requirements. This protocol should not serve as a substitute for acumen, but as a guide and a source of discussion in the management of pain which must be, in the end, individualized.

Clinical Case Discussion

Case: The patient is a 27-year-old male who was stabbed at the base of the neck and thrown off the top of a three story building. He arrives in the emergency room intoxicated, but awake and alert. He is hemodynamically stable. His past medical history is noncontributory. He is extremely tachypneic, anxious and complaining of shortness of breath. He is coughing up a small amount of blood. He is wearing a cervical collar. On secondary survey he is found to have subcutaneous emphysema.

Questions

- What are the anesthesiologists concerns?
- Should any further imaging be obtained prior to intubation?
- What airway device should be placed?
- What technique should be used to intubate the patient?

Given the mechanism of injury and the presence of subcutaneous emphysema and hemoptysis, the anesthesiologist should be concerned that there is an injury to the airway. While under ideal conditions an awake fiberoptic optic intubation would be preferred, the scenario presented describes a patient who is in respiratory distress and could not be expected to participate in an awake fiberoptic intubation. No further imaging should be necessary in this patient who clearly needs urgent control of the airway. Rapid sequence intubation with inline stabilization remains the standard of care and should be performed without delay. Strict attention should be made to the patient's hemodynamics after intubation, since converting a presumed pneumothorax to a tension pneumothorax is possible in this scenario. Every attempt must be made to place the endotracheal tube with great care in an effort not to disrupt a potential injury to the trachea.

Scenario continues: The patient is successfully intubated, and a chest tube is placed for decreased breath sounds over the right chest. A large air leak is found. CXR as shown in Fig. 40.4 is obtained.

Questions

- What would be the next step in the evaluation of this patient?
- How can the anesthesiologist manage the air leak?
- The patient is being taken to the operating room for surgical repair via right thoracotomy. What form of lung isolation should be used?

FIG. 40.3. Example of rib fracture protocol adapted from the one in use at Rhode Island Hospital. Non invasive (asterisk) protocol includes the use of a narcotic PCA, NSAIDs, acetaminophen and consideration of other modalities including dexmedetomidine infusion. *IS* incentive spirometry. Therapep® is a commercially available device that uses positive expiratory pressure to help minimize atelectasis and clear secretions. Acapella® is also a commercially available device that uses vibratory therapy and positive expiratory pressure to help clear secretions. EzPep® uses the coanda effect to produce a positive airway pressure throughout the entire respiratory cycle (inspiration, breath hold, and expiration). The goal of this device is to decrease atelectasis, increase inspiratory volume and clear secretions. It can also deliver aerosolized medications.

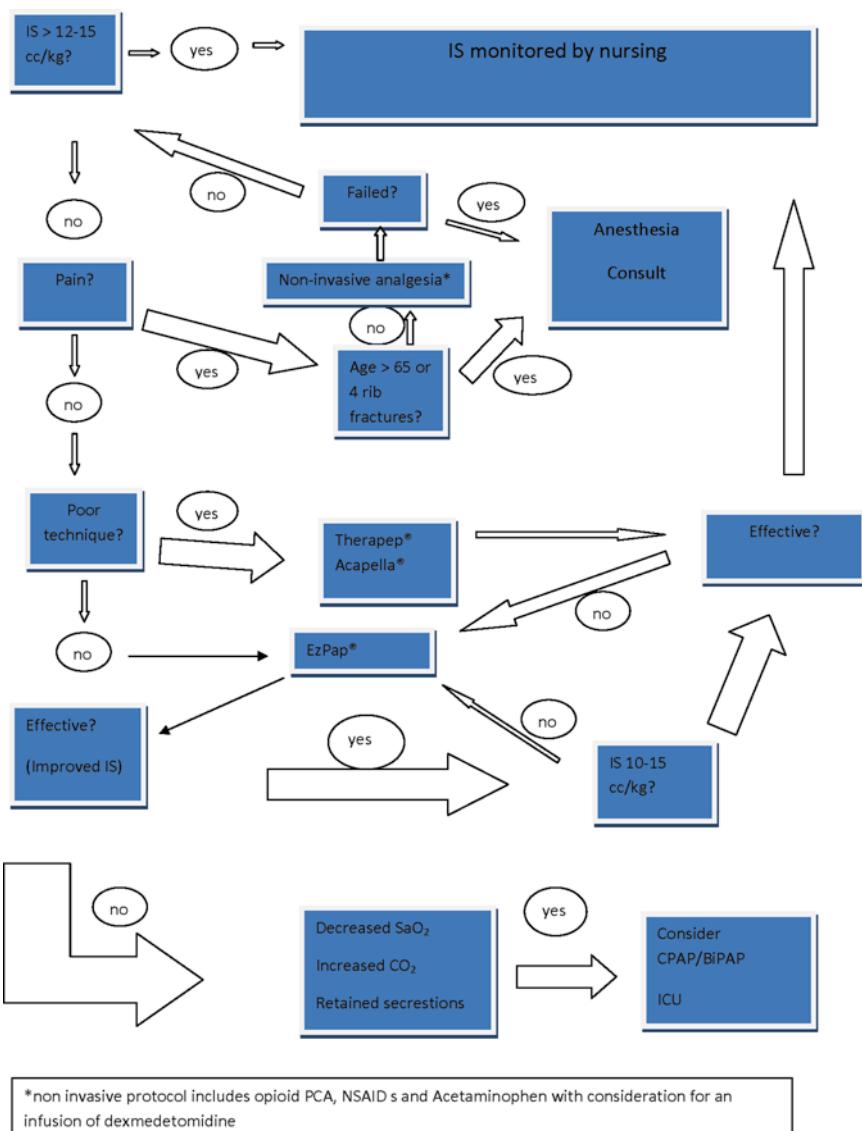


FIG. 40.4. Chest X-ray shows a patient with a persistent R pneumothorax despite well-positioned thoracostomy tube and an endotracheal tube just above the carina.

The patient should undergo fiberoptic bronchoscopy to define the tracheal injury and if possible to move the cuff of the endotracheal tube beyond the tear. This patient also underwent computed tomography which revealed a posterior tear in the trachea. The CT also demonstrated continued pneumothorax on the right as well as subcutaneous air. Lastly the CT (Fig. 40.5) demonstrated five posterior rib fractures on the right.

The first choice for lung isolation in this case would be a bronchial blocker through the original endotracheal tube. This would prevent any further tracheal injury by passing a larger stiffer device through the injury. In addition, the patient has not had injury to the cervical spine ruled out, and this will minimize movement of the neck. He is taken to the operating room for repair of this injury shown in Fig. 40.6.

Questions

- Would you extubate this patient at the end of the case?
- How would you control his pain from the rib fractures?



FIG. 40.5. Computed tomography scan demonstrating posterior tracheal tear, subcutaneous emphysema and persistent right pneumothorax.

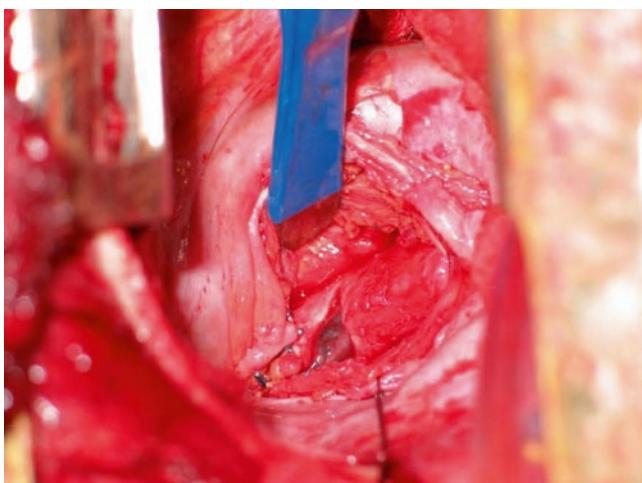


FIG. 40.6. Intraoperative view of posterior tracheal injury seen through a right thoracotomy (photo courtesy of Thomas NG, MD, thoracic surgery, Rhode Island Hospital).

These are both difficult questions. In general, every effort to extubate the patient as soon as possible should be made given his tracheal repair. Managing the pain of his rib fractures may be difficult. If he is awake and cooperative post extubation, an epidural can be considered. If not, paravertebral blocks or a catheter may be an option since the rib fractures are unilateral.

References

1. American College of Surgeons Committee on Trauma. Thoracic trauma. In: ATLS® program for doctors student course manual. 6th ed. Chicago: American College of Surgeons. 1997;127–141.
2. Bergen G, Chen LH, Warner M, Fingerhut LA. Injury in the United States: 2007 Chartbook. Hyattsville, MD: National Center for Health Statistics; 2008.
3. Fingerhut LA, Warner M. Injury Chartbook. Health, United States, 1996–1997. Hyattsville, MD: National Center for Health Statistics; 1998.
4. Rozynski GS, Feliciano DV, Ochsner MG, et al. The role of ultrasound in patients with possible penetrating cardiac wounds: a prospective multicenter study. *J Trauma*. 1999;46:543–51.
5. Kirkpatrick AW, Ball CG, D'Armours SK, Zygun D. Acute resuscitation of the unstable adult trauma patient: bedside diagnosis and therapy. *Can J Surg*. 2008;51(1):57–69.
6. Hakuba T, Minato N, Minematsu T, Kamohara K. Surgical management and treatment of traumatic right atrial rupture. *Gen Thorac Cardiovasc Surg*. 2008;56(11):551–4.
7. Lim R, Gill IS, Temes RT, Smith CE. The use of adenosine for repair of penetrating cardiac injuries: a novel method. *Ann Thorac Surg*. 2001;71:1714–5.
8. Santoni BG, Hindman BJ, Putt CM, Weeks JB, Johnson N, Maktabi MA, et al. Manual in-line stabilization increases pressures applied by the laryngoscope blade during direct laryngoscopy and orotracheal intubation. *Anesthesiology*. 2009;110:24–31.
9. Manoach S, Paladino L. Laryngoscopy force, visualization and intubation failure in acute trauma. *Anesthesiology*. 2009; 110:6–7.
10. Rice MJ, Mancuso AA, Gibbs C, Morey TE, Gravenstein N, Deitte LA. Cricoid pressure results in compression of the post-cricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg*. 2009;109:1546–52.
11. Ovassapian A, Salem MR. Sellick's Maneuver: to do or not to do. *Anesth Analg*. 2009;109:1360–2.
12. Lerman J. On cricoid pressure: “May the force be with you”. *Anesth Analg*. 2009;109:1363–6.
13. Priebe HJ. Cricoid pressure: an alternative view. *Semin Anesth*. 2005;24(2):120–6.
14. Wilson WC. Trauma: airway management. *ASA Newslett*. 2005;69(11):9–16.
15. Crosby ET. Airway management in adults after cervical spine trauma. *Anesthesiology*. 2006;104:1293–318.
16. Shatney CH, Brunner RD, Nguyen TQ. The safety of orotracheal intubation in patients with unstable cervical spine fracture or high spinal cord injury. *Am J Surg*. 1995;170:676–80.
17. Stephens CT, Kahnroff S, Dutton RP. The success of emergency endotracheal intubation in trauma patients: A 10-year experience at a major adult trauma referral center. *Anesth Analg*. 2009;109:866–72.
18. Campos JH, Hallam EA, Van Natta T, Kernstine KH. Devices for lung isolation used by anesthesiologists with limited thoracic experience. *Anesthesiology*. 2006;104:261–6.
19. Ehrenfeld JM, Walsh JL, Sandberg WA. Right- and Left-sided Mallinckrodt double-lumen tubes have identical clinical performance. *Anesth Analg*. 2008;106:1847–52.
20. Narayanaswamy M, McRae K, Slinger P, Dugas G, Kanellakos GW, Roscoe A, et al. Choosing a lung isolation device for

- thoracic surgery: a randomized trial of three bronchial blockers and double lumen tubes. *Anesth Analg.* 2009;108:1097–101.
21. Kirsh MM, Orringer MB, Behrendt DM, Sloan H. Management of tracheobronchial disruption secondary to non-penetrating trauma. *Ann Thorac Surg.* 1976;22:93–101.
 22. Kummer C, Netto FS, Rizoli S, Yee D. A review of traumatic airway injuries: potential implications for airway assessment and management. *Injury.* 2007;38:27–33.
 23. Rossbach MM, Johnson SB, Gomez MA, Sako EY, Miller L, Calhoun JH. Management of tracheobronchial injuries: a 28-year experience. *Ann Thorac Surg.* 1998;65:182–6.
 24. Kissner AC, Obrien SM, Detterbeck FC. Blunt tracheobronchial injuries: treatment and outcomes. *Ann Thorac Surg.* 2001;71:2059–65.
 25. Shah AS, Forbess JM, Skaryak LA, Lilly RE, Vaslef SN, D'Amico TA. Emergent thoracotomy for airway control after intrathoracic tracheal injury. *J Trauma.* 2000;48(6):1163–4.
 26. Naghibi K, Hashemi SL, Sajedi P. Anesthetic management of tracheobronchial rupture following blunt chest trauma. *Acta Anaesthesiol Scand.* 2003;47:901–3.
 27. Symbas PN, Justicz AG, Ricketts RR. Rupture of the airways from blunt trauma: treatment of complex injuries. *Ann Thorac Surg.* 1992;54:177–83.
 28. Shweikh AM, Nadkarni AB. Laryngotracheal separation with pneumopericardium after a blunt trauma to the neck. *Emerg Med J.* 2001;18:410–1.
 29. Gómez-Caro A, Ausín P, et al. Role of conservative medical management of tracheobronchial injuries. *J Trauma.* 2006;61:1426–35.
 30. Borasio P, Arissone F, Chiampo G. Post-intubation tracheal rupture. A report on ten cases. *Eur J Cardiothorac Surg.* 1997;12:98–100.
 31. Parmley LF, Mattingly TW, Manion WC, Jahnke Jr EJ. Non-penetrating traumatic injury of the aorta. *Circulation.* 1958;17:1086–101.
 32. Schulman CI, Carvajal D, Lopez PP, Soffer D, Habib F, Augenstein J. Incidence and crash mechanisms of aortic injury during the past decade. *J Trauma.* 2007;62:664–7.
 33. Neschis DG, Scalea TM, Flinn WR, Griffith BP. Blunt aortic injury. *N Engl J Med.* 2008;359:1708–16.
 34. Fabian TC, Richardson JD, Croce MA, Smith Jr JS, Rodman Jr G, Kearney PA, et al. Prospective study of blunt aortic injury: multicenter trial of the American Association for the surgery of trauma. *J Trauma.* 1997;42:374–80.
 35. Fabian TC, Davis KA, Gavant ML, et al. Prospective study of blunt aortic injury; helical CT is diagnostic and antihypertensive therapy reduces rupture. *Ann Surg.* 1998;227:666–76.
 36. Malhotra AK, Fabian TC, Croce MA, Weinman DS, Gavant ML, Pate JW. Minimal aortic injury: a lesion associated with advancing diagnostic techniques. *J Trauma.* 2001;51:1042–8.
 37. Hirose H, Gill IS, Malangoni MA. Nonoperative management of traumatic aortic injury. *J Trauma.* 2006;60:597–601.
 38. Coselli JS, LeMaire SA, Köksoy C, Schmittling ZC, Curling PE. Cerebrospinal fluid drainage reduces paraplegia after thoracoabdominal aortic aneurysm repair: results of a randomized clinical trial. *J Vasc Surg.* 2002;35:631–9.
 39. Ehrlich MP, Rousseau H, Heijman R, Piquet P, Beregi JP, Nienaber CA, et al. Early outcome of endovascular repair of acute traumatic aortic injuries: the talent thoracic retrospective registry. *Ann Thorac Surg.* 2009;88:1258–66.
 40. Lettinga-vandePoll T, Schurink GWH, DeHaan MW, Verbruggen JPAM, Jacobs MJ. Endovascular treatment of traumatic rupture of the thoracic aorta. *Br J Surg.* 2007;94:525–533.
 41. Feezor RJ, Hess PJ, Martin TD, Klodell CT, Beaver TM, Lottenberg L, et al. Endovascular treatment of traumatic aortic injuries. *J Am Coll Surg.* 2009;208:510–6.
 42. Reed AB, Thompson JK, Grafton CJ, Delvecchio C, Giglia JS. Timing of endovascular repair of blunt traumatic thoracic transections. *J Vasc Surg.* 2006;43:684–8.
 43. Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the surgery of trauma multicenter study. *J Trauma.* 2008;64:561–70.
 44. Demetriades D, Velmahos GC, Scalea TM, et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. *J Trauma.* 2008;64:1415–8.
 45. Devitt JH, McLean RF, Koch JP. Anaesthetic management of acute blunt thoracic trauma. *Can J Anaesth.* 1991;30:506–10.
 46. Leone M, Brégeon F, Antonini F, et al. Long term outcome in chest trauma. *Anesthesiology.* 2008;109:864–71.
 47. Soldati G, Testa A, Silva FR, et al. Chest ultrasonography in lung contusion. *Chest.* 2006;130:533–8.
 48. Ball CG, Ranson MK, Rodriguez-Galvez M, Lall R, Kirkpatrick AW. Sonographic depiction of posttraumatic alveolar-interstitial disease: the hand held diagnosis of a pulmonary contusion. *J Trauma.* 2009;66:962.
 49. Hoth JJ, Stitzel JD, Gayzik S, Brownlee NA, Miller PR, Yoza BK, et al. The pathogenesis of pulmonary contusion: an open chest model in the rat. *J Trauma.* 2006;61:32–45.
 50. Keel M, Ecknauer E, Stocker R, et al. Different pattern of local and systemic release of proinflammatory and anti-inflammatory mediators in severely injured patients with chest trauma. *J Trauma.* 1996;40:907–12.
 51. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury.* 2005;36:691–709.
 52. Muehlstedt SG, Richardson CJ, Lyte M, Rodriguez JL. Systemic and pulmonary effector cell function after injury. *Crit Care Med.* 2002;30:1322–6.
 53. Perl M, Gebhard F, Brückner UB, Ayala A, Braumüller C, Kinzl L, et al. Pulmonary contusion causes impairment of macrophage and lymphocyte immune function and increases mortality associated with a subsequent septic challenge. *Crit Care Med.* 2005;33(6):1351–8.
 54. Knöferl MW, Liener UC, Perl M, et al. Blunt chest trauma induces delayed splenic immunosuppression. *Shock.* 2004;22:51–6.
 55. Simon B, Ebert J, Bokhari F, Capella J, Emhoff T, et al. EAST practice management workgroup for pulmonary contusion-flail chest. Eastern association for the surgery of trauma. 2006. www.east.org/tpp/pulmcontflailchest.pdf. Accessed 1 Jan 2010.
 56. Schreiter D, Reske A, Stichert B, Seiwerts M, et al. Alveolar recruitment in combination with sufficient positive end-expiratory pressure increases oxygenation and lung aeration in patients with severe chest trauma. *Crit Care Med.* 2004;32(4):968–75.
 57. Kelly ME, Miller PR, Greenshaw JJ, Fabian TC, Proctor KG. Novel Resuscitation strategy for pulmonary contusion after severe chest trauma. *J Trauma.* 2003;55:94–105.
 58. Orlaguet G, Ferjani M, Riou B. The heart in blunt trauma. *Anesthesiology.* 2001;95:544–8.

59. Maron BJ, Gohman TE, Kyle SB, Estes NA, Link MS. Clinical profile and spectrum of commotion cordis. *JAMA*. 2002; 287:1142–6.
60. Link MS, Wang PJ, Pandian NG, et al. An experimental model of sudden death due to low-energy chest-wall impact (commotion cordis). *N Engl J Med*. 1998;338:1805–11.
61. Robert E, de la Coussaye JE, Aya AGM, Bertinchant JP, Polge A, Fabbro-Péray P, et al. Mechanisms of ventricular arrhythmias induced by myocardial contusion. *Anesthesiology*. 2000;92: 1132–43.
62. Sakka SG, Huettermann E, Giebe W, Reinhart K. Late cardiac arrhythmias after blunt chest trauma. *Intensive Care Med*. 2000;26:792–5.
63. Teixeria PG, Georgiou C, Inaba K, et al. Blunt cardiac trauma: lessons learned from the medical examiner. *J Trauma*. 2009;67:1259–64.
64. Sisley AC, Rozycski GS, Ballard RN, et al. Rapid detection of traumatic effusion using surgeon performed ultrasonography. *J Trauma*. 1998;44(2):291–6.
65. Rozycski GS, Feliciano DV, Oschner MG, et al. The role of surgeon performed ultrasound in patients with possible cardiac wounds. *Ann Surg*. 1996;223(6):737–44.
66. Pasquale MD, Nagy K, Clark J. Practice management guidelines for the screening of blunt cardiac injury; Eastern Association for the Surgery of Trauma: 1998. Available on URL www.east.org/tpp/chap2.pdf. Accessed 1 Jan 2010.
67. Christensen MA, Sutton KR. Myocardial contusion: new concepts in diagnosis and management. *Am J Crit Care*. 1993;2(1):28–34.
68. Lindstaedt M, Germing A, Lawo T, et al. Acute and long-term clinical significance of myocardial contusion following blunt thoracic trauma: results of a prospective study. *J Trauma*. 2002;52:479–85.
69. Velmahos GC, Karaiskakis M, Salim A, Toutouzas KG, Murray J, Asensio J, et al. Normal electrocardiography and serum troponin I levels preclude the presence of clinically significant cardiac injury. *J Trauma*. 2003;54:45–51.
70. Maenza RL, Seaberg D, D'Amico F. A meta-analysis of blunt cardiac trauma: ending myocardial confusion. *Am J Emerg Med*. 1996;14:237–41.
71. Schultz JM, Trunkey DD. Blunt cardiac injury. *Crit Care Clin*. 2004;20(1):57–70.
72. Parmley LF, Manion WC, Mattingly TW. Nonpenetrating traumatic injury to the heart. *Circulation*. 1958;18(3):371–96.
73. Jeon Y, Ryu JH, Lim YJK, Kim CSB, Bahk JH, Yoon SZ, et al. Comparative effects of vasopressin and norepinephrine after milrinone-induced hypotension in off-pump coronary artery bypass surgical patients. *Eur J Cardiothoracic Surg*. 2006;29(6):952–6.
74. Ziegler DW, Agarwal NN. The morbidity and mortality of rib fractures. *J Trauma*. 1994;37(6):975–9.
75. Clark GC, Schechter WP, Trunkey DD. Variables affecting outcome in blunt chest trauma: flail chest vs. pulmonary contusion. *J Trauma*. 1988;28:298–304.
76. Barnea Y, Kashtan H, Shornick Y, Werbin N. Isolated rib fractures in elderly patients; mortality and morbidity. *Can J Surg*. 2002;45:43–6.
77. Bulger EM, Arenson MA, Mock CN, Jurkovich GJ. Rib fractures in the elderly. *J Trauma*. 2000;48(6):1040–7.
78. Simon BJ, Cushman J, Barraco R, for the EAST Practice Management Guidelines work Group, et al. Pain management guidelines for blunt thoracic trauma. *J Trauma*. 2005;59:1256–67.
79. Mackersie RC, Karagianes TG, Hoyt DB, Davis JW. Prospective evaluation of epidural and intravenous administration of fentanyl for pain control and restoration of ventilator function following multiple rib fractures. *J Trauma*. 1991;31(4):443–51.
80. Knottenbelt JD, James MF, Bloomfield M. Intrapleural bupivacaine analgesia in chest trauma: a randomized double-blind controlled trial. *Injury*. 1991;22(2):114–6.
81. Lunchette FA, Radafshar SM, Kaiser R, Flynn W, Hassett JM. Prospective evaluation of epidural versus intrapleural catheters for analgesia in chest wall trauma. *J Trauma*. 1994;36(6): 865–70.
82. Short K, Scheeres D, Mlakar J, et al. Evaluation of intrapleural analgesia in the management of blunt traumatic chest wall pain: a clinical trial. *Am Surg*. 1996;62:488–93.
83. el-Baz N, Faber LP, Ivankovich AD. Intrapleural infusion of local anesthetic: a word of caution. *Anesthesiology*. 1988;68:809–10.
84. Lauder GR. Interpleural analgesia and phrenic nerve palsy. *Anaesthesia*. 1993;48:315–6.
85. Parkinson SK, Mueller JB, Rich TJ, Little WL. Unilateral Horner's syndrome associated with interpleural catheter injection of local anesthetic. *Anesth Analg*. 1989;68:61–2.
86. Shinohara K, Iwama H, Akama Y, Tase C. Interpleural block for patients with multiple rib fractures: comparison with epidural block. *J Emerg Med*. 1994;12:441–6.
87. Karmakar MK, Ho AM. Acute pain management of patients with multiple fractured ribs. *J Trauma*. 2003;54:615–25.
88. Moore KL, Dalley AF. Thorax. In: Kelly PJ, editor. Clinically oriented anatomy. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999. p. 59–173.
89. Pedersen VM, Schulze S, Hoier-Madsen K, Halkier E. Air flow meter assessment of the effect of intercostals nerve blockade on respiratory function in rib fractures. *Acta Chir Scand*. 1983;149:119–20.
90. Toledo-Pereyra LH, DeMeester TR. Prospective randomized evaluation of intrathoracic nerve block with bupivacaine on post-operative ventilator function. *Ann Thor Surg*. 1979;27:203–5.
91. Kaplan JA, Miller ED, Gallagher EG. Postoperative analgesia of thoracotomy patients. *Anesth Analg*. 1975;54:773–7.
92. Shanti CM, Carlin AM, Tyburski JG. Incidence of pneumothorax from intercostals nerve blocks for analgesia in rib fractures. *J Trauma*. 2001;51:536–9.
93. Baxter AD, Flynn JF, Jennings FO. Continuous intercostal nerve blockade. *Br J Anaesth*. 1984;56:665–6.
94. Mowbray A, Wong KK, Murray JM. Intercostal catheterization; an alternative approach to the paravertebral space. *Anaesthesia*. 1987;42:959–61.
95. Slinger P. informal poll taken at thoracic conference. Houston, TX: MD Anderson Cancer cente; 2008.
96. Gerner P. Postthoracotomy pain management problems. *Anesthesiol Clin*. 2008;26:355–67.
97. Conlon NP, Shaw AD, Grichnik KP. Postthoracotomy paravertebral analgesia: will it replace epidural analgesia? *Anesthesiol Clin*. 2008;26:369–80.
98. Mohta M, Verma P, Saxena AK, Sethi AK, Tyagi A, Girotra G. Prospective, randomized comparison of continuous thoracic epidural and thoracic paravertebral infusion in patients with unilateral multiple fractured ribs- a pilot study. *J Trauma*. 2009;66:1096–101.
99. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade

- for thoracotomy- a systematic review and meta-analysis of randomized trials. *Br J Anaesth.* 2006;96:418–26.
100. Karmakar MK, Critchley LAH, Ho AMH, Gin T, Lee TW, Yin APC. Continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with multiple fractured ribs. *Chest.* 2003;123:424–31.
101. Bulger EM, Edwards T, Klotz P, Jurkovich GJ. Epidural analgesia improves outcome after multiple rib fractures. *Surgery.* 2004;136:426–30.
102. Shibata Y, Nishiwaki K. Ultrasound-guided intercostals approach to thoracic paravertebral block. *Anesth Analg.* 2009;109(3):996–7.
103. Ben-Ari A, Moreno M, Chelly JE, Bigeleisen PE. Ultrasound-guided paravertebral block using an intercostals approach. *Anesth Analg.* 2009;109(5):1691–4.
104. Hara K, Sakura S, Nomura T, Saito Y. Ultrasound guided thoracic paravertebral block in breast surgery. *Anaesthesia.* 2009;64(2):223–5.
105. Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. *Anaesthesia.* 1995;50(9):813–5.
106. Evans PJ, Lloyd JW, Wood GJ. Accidental intrathecal injection of bupivacaine and dextran. *Anaesthesia.* 1981;36:685–7.
107. Sharrock NE. Postural headache following thoracic somatic paravertebral block. *Anesthesiology.* 1980;52:360–2.
108. Worthley LI. Thoracic epidural management of chest trauma. *Intensive Care Med.* 1985;11:312–5.
109. Ullman DA, Wimpy RE, Fortune JB, Kennedy TM, Greenhouse BB. The treatment of patients with multiple rib fractures using continuous thoracic epidural narcotic infusion. *Regional Anesth.* 1989;14:43–7.
110. Dittman M, Keller R, Wolff G. A rationale for epidural analgesia in the treatment of multiple rib fractures. *Intensive care med.* 1978;4:193–7.
111. Ueda K, Ueda W, Manabe M. A comparative study of sequential epidural bolus technique and continuous epidural infusion. *Anesthesiology.* 2005;103:126–9.
112. Halpern SH, Carvalho B. Patient-controlled epidural analgesia for labor. *Anesth Analg.* 2009;108:921–8.
113. Joshy GP, Bonnet F, Shah R, Wilkinson RC, Camu F, et al. A systematic review of randomized trials evaluating regional techniques for Postthoracotomy analgesia. *Anesth Analg.* 2008;107:1026–40.
114. Moon MR, Luchette FA, Gibson SW, et al. Prospective, randomized comparison of epidural versus parenteral opioid analgesia in thoracic trauma. *Ann Surg.* 1999;229:684–91.

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Anesthetic Management of Post-Thoracotomy Complications

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Key Points

- The immediate postoperative period following thoracic surgery is a dynamic time characterized by rapidly changing physiology. Anesthetic and surgically related complications may become evident and may require immediate intervention.
- Although most patients undergoing thoracic surgery are extubated immediately following surgery, preexisting lung disease may necessitate postoperative mechanical ventilation. Patients remaining intubated postoperatively should be assessed frequently for extubation and ventilator modes utilized that promote spontaneous ventilation and low airway pressures.
- Airway-related complications are not uncommon and may be due to anesthetic or surgical technique. The large caliber of double lumen endotracheal tubes may increase the risk of airway injury. Vocal cord palsies and airway bleeding may also occur.
- Intrathoracic complications range from relatively minor air leaks to life-threatening bronchopleural fistulas. Preoperative prophylaxis against deep venous thrombosis helps prevent pulmonary embolism. Other complications such as phrenic nerve injury may become evident immediately postoperatively or after a prolonged period of mechanical ventilation in the ICU.
- Atrial fibrillation is a very common complication following thoracic surgery. Its management depends on the patient's

hemodynamic status. New onset atrial fibrillation should prompt a thorough review of the patient's overall wellbeing. Other cardiac complications are less common, including cardiac herniation and interatrial shunting.

Introduction

The immediate postoperative period following thoracotomy is characterized by rapidly changing physiology, during which careful management and attention to possible surgical or anesthetic complications is necessary. The normal physiological changes associated with emergence from anesthesia and mechanical ventilation may be less predictable in a patient having just undergone thoracic surgery. Patients undergoing thoracic procedures often have multiple comorbidities and poor baseline lung function. The surgeries are often long, may be associated with significant blood loss, and risk damage to intrathoracic structures including the lungs, airway, and peripheral nervous system. Thoracic surgery may also cause significant stress on the cardiovascular system. Many factors may preclude the patient's immediate liberation from mechanical ventilation, and anesthetic or surgical complications may become evident in the operating room or shortly after arrival in the recovery room or intensive care unit (ICU). In this chapter, we will explore some of the common management challenges and potential complications that may be encountered in the immediate postoperative period following thoracotomy.

Mechanical Ventilation and Extubation

Classification of Respiratory Failure

The decision regarding tracheal extubation of a patient following surgery must take into account many variables. Patients requiring mechanical ventilation all have respiratory failure that falls into one (or more) of four categories:

1. *Type I* (hypoxemic respiratory failure) is characterized by $\text{PaO}_2 < 60 \text{ mmHg}$ at sea level.
2. *Type II* (hypercapnic respiratory failure) is characterized by $\text{PaCO}_2 > 45 \text{ mmHg}$.
3. *Type III* (perioperative respiratory failure) is due to increased atelectasis and low functional residual capacity (FRC). This may occur in the setting of abnormal respiratory muscle mechanics, and may precipitate Types I or II failure.
4. *Type IV* (respiratory failure secondary to shock) may be present when mechanical ventilation is utilized to decrease oxygen consumption and increase oxygen delivery in the setting of resuscitation and shock.

Criteria for Extubation

Patients having just undergone thoracic surgery may experience any of these types of respiratory failure, although Types I, II and III are more likely than Type IV. All patients emerging from anesthesia who require continued mechanical ventilation suffer, to some extent, from Type III failure. Even patients with healthy lungs experience hypoxemia secondary to airway closure and atelectasis [1]. Indeed, collapsed lung tissue is observed in 90% of patients under anesthesia [2]. Residual anesthetics and neuromuscular blocking agents may also contribute to hypoventilation and subsequent hypoxemia and hypercarbia. In patients requiring one lung ventilation for thoracic surgery, changes in ventilation and perfusion may be even more pronounced, and hypoxia more frequent. While recruitment maneuvers on the ventilator may be useful to expand portions of collapsed lung tissue [2], patients with poor baseline lung function may not tolerate extubation at the conclusion of surgery because of hypoxia, and a combination of Types I and III respiratory failure. These patients may require continued mechanical ventilation postoperatively until adequate gas exchange can be reestablished.

Patients may also fail extubation due to impaired CO_2 removal. In the case of thoracic surgery, pain from a thoracotomy incision may prevent deep breathing and adequate CO_2 elimination. Epidural analgesia is very effective at controlling post-thoracotomy pain and minimizing postoperative hypercarbia. In cases where thoracotomy is unplanned, epidural placement at the end of surgery, or shortly after extubation, may help reduce the need for reintubation.

Complications of Prolonged Intubation and Mechanical Ventilation

In 2001, a task force (represented by the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine) established guidelines for the assessment and implementation of discontinuation of patients from mechanical ventilation [3]. These guidelines call for evidence of resolution of the underlying cause of respiratory failure, adequate oxygenation ($\text{PaO}_2/\text{FiO}_2 > 150-200$, $\text{PEEP} \leq 5-8 \text{ cmH}_2\text{O}$, $\text{FiO}_2 \leq 0.4-0.5$), adequate pH (≥ 7.25), hemodynamic stability, and the capability to initiate spontaneous ventilation. Patients meeting these criteria may then undergo a formal spontaneous breathing trial (SBT) for 30–120 min.

Those who successfully pass an SBT have a high likelihood of tolerating extubation, and assessment of the ability to protect the airway, mental status, and likelihood of airway obstruction should be performed prior to removal of the endotracheal tube [4]. Although not a guarantee, an intact gag reflex and alert state of mind suggest the patient will be able to protect the airway against aspiration. This may not be true in the case of vocal cord injury, however. Aspiration risk may be better assessed after extubation via a flexible endoscopic evaluation of swallowing with sensory testing (FEESST) examination.

While extubation in the immediate postoperative period requires fulfilling many of these same criteria, emergence from anesthesia is a rapid and dynamic process and assessment of these variables may be made on a minute-to-minute basis. Other variables are also assessed, including tidal volume (desire 5–10 cc/kg), respiratory rate (≤ 20 breaths/min), body temperature, electrolytes, and volume status.

When comparing predictors of a successful extubation, two useful tests are the rapid shallow breathing index (RSBI, respiratory rate/tidal volume), and the negative inspiratory force (NIF). While an $\text{NIF} > 20 \text{ cmH}_2\text{O}$ does not guarantee a successful extubation, a poor performance in this test usually predicts failure [5]. In a review of studies of factors associated with ventilator weaning, a $\text{RSBI} < 105 \text{ breaths/min/L}$ had a sensitivity up to 96%, and specificity up to 73% for prediction of a successful extubation [6].

Provided the necessary criteria are met, and there are no plans for further surgery over the next 24–48 h, there are few reasons to delay extubation. In patients undergoing pulmonary surgery, a prompt transition from positive pressure ventilation to spontaneous breathing is usually desirable in light of new suture lines or staples within the tracheobronchial tree. In practice, the majority of patients undergoing thoracic surgery are extubated in the operating room.

Independent Lung Ventilation

In a retrospective study of 214 patients undergoing lung transplantation, intubation greater than 72 h was identified as an

independent risk factor for airway complications [7], and early postoperative extubation may help reduce this risk [8]. Following esophagectomy, early extubation has been shown to be safe and lead to short ICU lengths of stay [9, 10]. Similarly, immediate extubation following tracheal surgery has yielded good results. In a retrospective review of 60 patients undergoing tracheal resection and reconstruction, all but one patient was successfully extubated in the operating room [11]. Likewise, extubation in the operating room immediately following lung resection has been shown to be safe, reduce the risk of postoperative complications, decrease time in the ICU, and reduce hospital costs [12].

Adverse effects associated with intubation and mechanical ventilation include ventilator-associated pneumonia (VAP), laryngeal and tracheal injury, hemodynamic changes, patient discomfort and the need for sedation, and difficulty obtaining an accurate neurologic examination [13].

While severe unilateral lung disease in the postoperative setting is uncommon, it may occur following single lung transplantation or pneumonectomy (Fig. 41.1). In the case of lung transplantation, independent lung ventilation in the ICU may be necessary to allow different ventilation strategies to each lung. Independent lung ventilation requires a double lumen endotracheal tube (DLT). DLT are rarely utilized outside of the OR as they are technically more difficult to manage, require constant attention to ensure proper position, and their larger size makes laryngeal and tracheal trauma more likely compared to single-lumen tubes. The narrower lumen can make it more difficult to perform bronchoscopy and endotracheal suctioning. Nevertheless, in cases of severe unilateral ARDS, as may occur after lung transplantation, the ability to provide different tidal volumes and oxygen concentrations to each lung may be critical to patient management.

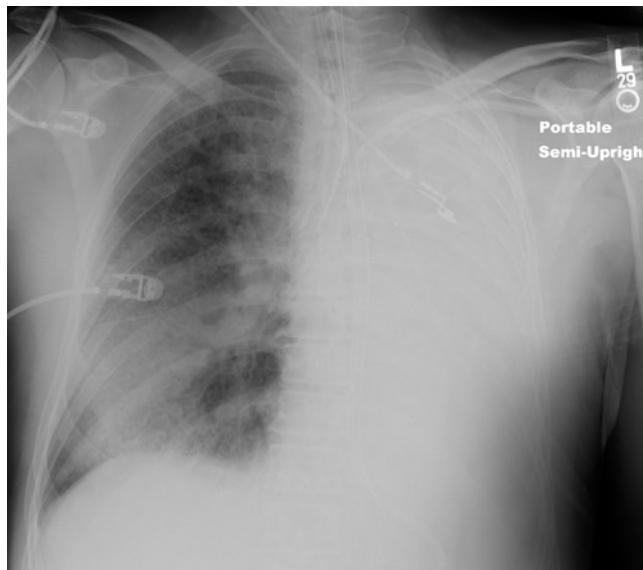


FIG. 41.1. Unilateral ARDS following left-sided pneumonectomy.

Airway Complications

Endotracheal Intubation and Airway Injury

Airway complications following thoracic surgery may be related to anesthetic or surgical technique. The larger external diameter and more invasive positioning of DLTs may increase the likelihood of airway trauma compared to a single-lumen ETT. Anesthetic-related airway complications that may become apparent immediately postoperatively include injury to dentition, sore throat, laryngeal trauma, bronchial erythema and edema, vocal cord injury, and tracheobronchial rupture (TBR). Risk factors associated with vocal cord injury include intubating conditions, type of surgery, and endotracheal tube size, among others [14].

In a study comparing DLT to bronchial blockers in patients undergoing pulmonary resection, the overall incidence of bronchial and vocal cord injury was 25 and 30%, respectively [14]. In both cases, the most common injuries were erythema and edema. Severe complications such as TBR are unusual, with an estimated incidence between 0.05 and 0.37% for all intubations at a single institution [15]. Symptoms of TBR include neck emphysema and hemoptysis.

Airway Bleeding and Secretions

The nature of the surgical procedures and proximity to structures vital to proper respiratory function make patients undergoing thoracic surgeries particularly prone to airway injuries and complications. Blood and secretions may accumulate in the upper or lower airways in patients undergoing lung resection surgery. Removal of blood by endotracheal suctioning may be difficult in a patient with a DLT, and a pediatric-sized bronchoscope may be necessary to pass through the tube's narrow lumen. If significant secretions and debris are present within the airways, changing the DLT to a larger diameter single-lumen ETT may better facilitate suctioning and lavage before extubation.

Vocal Cord Injuries

Vocal cord palsies may occur in patients undergoing mediastinoscopy or esophagectomy, with an incidence between 1–6 and 5–22% respectively [16]. Damage to the recurrent laryngeal nerve may occur intraoperatively from traction in the anterior mediastinum [16], or from direct trauma to the nerve. Unilateral vocal cord paralysis may result in voice changes, but usually does not result in airway obstruction. While bilateral vocal cord injury is rare except in the case of neck surgery, it has been reported following lung resection under VATS [17]. In this case report, vocal cord injury may have resulted from the DLT. Bilateral vocal cord injury may lead to dyspnea, stridor, and increased risk of aspiration.

Prompt recognition of vocal cord paralysis in the extubated patient is critical to prevent a potentially life-threatening situation. While a hoarse voice is relatively common after endotracheal intubation, the presence of stridor or respiratory distress is abnormal, and a sign indicating a more serious process may be occurring. Prompt intubation may be the safest approach to the patient in acute, severe respiratory distress, particularly if it presents in the immediate postoperative period. However, it is difficult to examine the vocal cords in an intubated patient.

If symptoms are mild and the patient remains stable, it is reasonable to treat the patient conservatively with oxygen by mask, steroids, and racemic epinephrine. The vocal cords may then be examined by flexible fiberoptic laryngoscopy in cases with a high clinical suspicion of vocal cord injury. Heliox is a mixture of helium and oxygen that has a lower viscosity than air (usually 70% helium and 30% oxygen). Because both airway diameter and the viscosity of the inspired gas both contribute to the work of breathing, treatment with lower viscosity heliox may reduce the effort required to breathe through partially closed vocal cords. Its effects may be seen very rapidly. Most studies of heliox are in the pediatric population.

Intrathoracic Complications

Patients requiring thoracic surgery are among the sickest patients in the hospital – many are diabetic, have chronic obstructive pulmonary disease (COPD), and coronary artery disease (CAD). Despite optimal preoperative evaluation and intraoperative technique, the high acuity of this patient population contributes to the significant rate of postoperative surgical complications. Common complications include persistent air leak, pneumothorax, and atrial fibrillation. Other complications include bronchopleural fistula (BPF), pulmonary embolism, postpneumonectomy syndrome, phrenic nerve injury, cardiac herniation, massive hemorrhage, mediastinal emphysema, and intracardiac shunting.

Air Leak, Pneumothorax, and Bronchopleural Fistula

Postoperative air leaks are common after thoracic surgery and can be easily recognized by the presence of bubbles in the water seal chamber of the drainage system. The presence of an air leak with a properly positioned chest tube indicates that air is passing from the pleural space into the drainage system. If the chest tube has been placed for a pneumothorax, an air leak signifies the pneumothorax is being successfully evacuated, and the leak should resolve as the pneumothorax improves.

Any surgery in which the pleural space is entered leads to the creation of a pneumothorax. A pneumothorax that remains in communication with atmospheric pressure is rarely dangerous. If it is not in communication with the atmosphere, a tension pneumothorax may develop. A tension pneumothorax may rapidly expand in a patient receiving positive pressure ventilation, leading to hemodynamic collapse.

When the lung parenchyma is cut, as in the case of a lobectomy, an air leak may be caused by small fistulas between the distal airways and the pleural space. This should resolve as the lung tissue heals and becomes apposed to the parietal pleura. In patients with COPD, a new air leak may be caused by rupture of a pulmonary bleb. An inadequate seal at the site of chest tube exit from the skin may also allow air to track back to the pleural space and communicate with the drainage system.

In the immediate postoperative period small air leaks rarely cause problems. In patients having undergone pneumonectomy, however, a large new air leak can indicate rupture of the bronchial stump and creation of a broncho-pleural fistula (BPF). There may be significant mediastinal shift toward the remaining lung, as well as subcutaneous emphysema. This is a surgical emergency that requires immediate attention. In a retrospective study of patients undergoing pneumonectomy, 1.9% developed BPF [18]. Two-thirds of these patients died. Ventilation for greater than 24 h was the only significant risk factor identified in this study. The diameter of the bronchial stump has also been associated with postpneumonectomy BPF [19].

While many pneumonectomy patients are extubated immediately after surgery in the operating room, it is not uncommon to remain intubated postoperatively in the ICU. A prompt extubation and transition from positive pressure to spontaneous ventilation is important to help reduce intrathoracic pressure. If a BPF does occur, and is associated with hemodynamic and respiratory instability, intubation with either a DLT or single-lumen ETT placed into the main stem bronchus is a reasonable approach to secure the airway. The latter approach is easier on the left side due to the greater distance between the carina and branching of the left upper and lower lobes. Again, spontaneous ventilation, or the use of very low inspiratory pressures, is desirable.

Mediastinal Emphysema

Mediastinal emphysema occurs when air accumulates in the mediastinal space. It may occur with alveolar or esophageal rupture, or following intrathoracic surgery. Patients may present with dyspnea or subcutaneous emphysema, and the diagnosis can be readily obtained with chest radiography or CT scan. Often, no treatment is necessary, although a chest tube may be placed if a pneumothorax is present. In the case of esophageal rupture, immediate surgical repair or esophageal stenting may be necessary.

Deep Venous Thrombosis and Pulmonary Embolism

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are potentially fatal complications that may follow thoracic surgery. In a review of 690 patients undergoing chest surgery for malignant lung disease, there were 12 (1.7%) venous thromboembolic complications, of which 9 (1.3%) were PE [20]. All events occurred in patients who were receiving DVT prophylaxis with heparin. Prolonged surgical times and malignancy

are risk factors for the development of DVT that are common to many patients undergoing thoracic surgery. Antithrombotic prophylaxis with heparin (either low molecular weight or unfractionated), has become common practice in the perioperative period and is likely responsible for fewer postoperative thrombotic complications.

A high index of suspicion is necessary to ensure detection of DVT and PE, as many PE are subclinical and only detected at autopsy. The initial chest radiograph is often normal in patients with PE. Pulmonary angiography represents the gold standard diagnostic technique. However, computed tomography angiography (CT angiogram) is easier to perform and is the most commonly employed technique for PE diagnosis. Ventilation–perfusion scans are less widely used as the results may be difficult to interpret. In the presence of a large PE with hemodynamic compromise, right ventricular dilatation and strain may be seen on echocardiogram.

When a clinically significant PE does occur, a variety of therapies may be employed including operative embolectomy [21], catheter embolectomy, systemic anticoagulation, or thrombolytic administration. The decision of how to proceed depends on a variety of factors including the size of the embolus, the location within the pulmonary vasculature, and the hemodynamic status of the patient.

Postpneumonectomy Syndrome

Postpneumonectomy syndrome is an uncommon condition that may be observed following left- or right-sided pneumonectomy [22]. It is characterized by mediastinal shift toward the side of the resected lung, with associated herniation of the overinflated remaining lung in the same direction. Subsequent compression of the distal trachea or main stem bronchus against the vertebral column or aorta may cause airway compression and obstruction [23].

Patients may present with progressive dyspnea, stridor, or heartburn and dysphagia if esophageal compression develops [22]. Symptoms develop months to years after a pneumonectomy. A high index of suspicion is necessary to make the diagnosis, which may be confirmed with a variety of techniques including awake bronchoscopy, pulmonary function tests, and CT scan. Treatment often involves mediastinal repositioning with expandable saline prostheses [24].

Post Lung Resection Pulmonary Edema

Post lung resection pulmonary edema is a serious complication that carries a mortality rate greater than 50% [25]. In a series of 146 patients who underwent pneumonectomy, mild to moderate noncardiogenic pulmonary edema was observed in 15% of patients, and was strongly associated with previous radiotherapy and excess intraoperative volume administration [26]. The incidence of pulmonary edema is higher following right pneumonectomy compared to left, with clinical symptoms typically appearing between POD 2–4. While an association with excess fluid administration exists, pulmonary

artery occlusion pressure (PAOP) is often low, suggesting a multifactorial etiology [25]. Pulmonary edema may also follow lobectomy, although this is less common.

Post lung resection pulmonary edema is a diagnosis of exclusion, and all other etiologies of pulmonary congestion must be ruled out (heart failure, pulmonary aspiration, sepsis, pulmonary embolism, transfusion reaction). As with cardiac herniation, a high level of suspicion is necessary to make the diagnosis. Once identified, treatment is largely supportive and may include high-dose corticosteroids and the use of pulmonary artery vasodilators [27] or extra-corporeal ventilatory support (see Chap. 43).

Phrenic Nerve Injury

Phrenic nerve injury may occur in patients undergoing thoracic surgery. Both hypothermia (associated with pericardial cooling in cardiac surgery) and mechanical trauma may be contributing factors [28]. Injury to the phrenic nerve is associated with diaphragmatic dysfunction. Unilateral diaphragmatic paralysis is often well tolerated by patients without significant underlying pulmonary disease [29]. However, thoracic surgery patients often have poor baseline lung function and difficulty weaning from the ventilator may be the first sign that phrenic nerve injury has occurred. An elevated hemidiaphragm may also be observed on chest radiography, and the diagnosis can be confirmed by electromyography. In severe cases, techniques such as diaphragmatic pacing may be useful [29]. Abnormal diaphragmatic motion postoperatively has been associated with diminished lung volumes and reduced exercise capacity [30].

Cardiac Complications

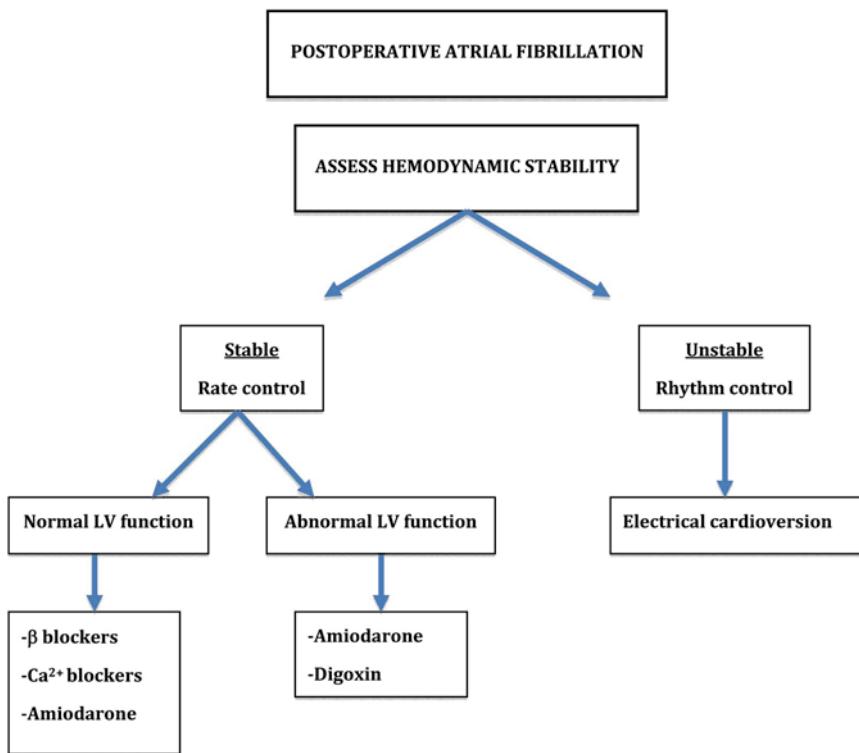
Cardiac Failure and Arrhythmias

Thoracic surgery represents a considerable stress on the cardiovascular system and postoperative cardiac complications are not uncommon. Patients often have preexisting cardiac disease and may be at risk for perioperative myocardial infarction (MI) and heart failure. Adequate preoperative evaluation and optimization of cardiac function may decrease these risks. In a patient with risk factors, postoperative hemodynamic instability should trigger suspicion of MI or acute heart failure.

Arrhythmias are the most common cardiac complication following thoracic surgery, with atrial fibrillation (AF) being the most prevalent. The incidence of AF may reach 20% after lobectomy and as high as 40% following pneumonectomy [31]. It is unclear whether postoperative supraventricular tachycardias (SVT) worsen patient outcome. In an observational study of 82 patients undergoing elective thoracotomy, there was no association between SVT and myocardial ischemia or adverse outcome [32].

AF complicating lung cancer resection has been associated with increased hospital length of stay, costs, and in-hospital mortality [33]. While AF is often relatively asymptomatic and

FIG. 41.2. Treatment algorithm for new onset postoperative atrial fibrillation.



easy to treat, its onset must not be ignored. Roselli and colleagues identified a temporal association between the onset of AF and other complications, particularly respiratory and infectious in etiology [33]. New onset AF in the immediate postoperative period should prompt a thorough review of the patient's overall condition.

Management of perioperative AF is well described in the literature and largely dictated by the patient's hemodynamic status (Fig. 41.2). The use of amiodarone in patients having undergone lung transplant is relatively common despite its potential pulmonary toxicity. Amiodarone-induced pulmonary toxicity correlates with total dose administered, and is more common after 2 months of therapy [34]. Judicious use in the perioperative period may be justified in the appropriate clinical situation.

Cardiac Herniation

Cardiac herniation is a rare and potentially lethal complication of thoracic procedures, most commonly occurring within 24 h following intrapericardial pneumonectomy [35]. Sudden hypotension and tachycardia should trigger the physician to consider the diagnosis. In the case of right-sided herniation, central venous pressure (CVP) may be elevated and cyanosis of the face and neck are common, and related to impaired venous drainage by the superior vena cava (SVC) [36]. This impaired drainage may reduce cardiac filling and lead to obstructive shock. Left-sided herniation can lead to myocardial ischemia and arrhythmias due to ventricular strangulation by the pericardial edges [37].

Herniation may be triggered by multiple factors. Positive intrathoracic pressure (due to coughing or mechanical ventilation), suction on a chest tube, or even patient repositioning may be contributing factors [37]. A prompt diagnosis is critical and may be obtained by chest radiography (easier to diagnose right-sided herniation than left), or echocardiogram. Immediate surgical repositioning of the heart and closure of the pericardial defect is necessary.

It should be noted that while cardiac herniation typically presents with rapidly deteriorating hemodynamics, this is not universally the case. Buniva and colleagues describe a patient in which cardiac herniation and torsion developed following right pneumonectomy and partial pericardectomy [38]. In this case, the patient remained hemodynamically stable and herniation was detected 2 h later on routine chest radiography. Herniation has also been reported 6 months following pneumonectomy [39], however, this is exceedingly uncommon. Adhesions between the heart and pericardium help prevent delayed herniation [37]. Along with the risk of bronchial stump rupture, the risk of cardiac herniation underscores the importance of a prompt transition to spontaneous ventilation in patients following pneumonectomy.

Interatrial Shunting

Interatrial shunting (right to left) is a rare cause of hypoxemia in patients having undergone pneumonectomy. The exact pathophysiology is poorly understood but may involve the development of a right- to left-sided pressure gradient, or decreased compliance of the right ventricle relative to the

left [40]. Shunting across an atrial septal defect (ASD) occurs primarily during diastole, and right to left blood flow may be accentuated by a stiffer right ventricle [40]. Case reports of shunting after pneumonectomy highlight three common features: a positional nature of the shunt, whereby it is worsened when the patient is upright (platypnea), an asymptomatic interval following surgery, and an increased shunt fraction with hypovolemia [41]. Diagnosis of interatrial shunting can be readily made by echocardiogram.

Clinical Case Discussion

A 67-year-old man is in the ICU 4 h following left-sided pneumonectomy for lung cancer. His medical history is significant for a 50-pack year smoking history and ischemic cardiomyopathy with a left ventricular ejection fraction of 30%. At the end of the surgery he was oxygenating poorly with a PaO_2 55 mmHg on 100% inspired oxygen, and is currently receiving mechanical ventilation in the ICU. His EKG changes from sinus rhythm to rapid atrial fibrillation with a heart rate 144 bpm, and his blood pressure falls to 60/40. You are called emergently to the bed side.

Questions

- What type of respiratory failure is this patient suffering from?
- Why is it important to extubate this patient and reestablish spontaneous ventilation in a timely fashion?
- How would you assess and treat this patient when you are called to the bedside?

Respiratory failure, extubation, and assessment of atrial fibrillation:

- Type III respiratory failure (perioperative), likely due to atelectasis from anesthesia and positive pressure ventilation, hypoxia and hypercarbia from baseline lung disease (see Sect. “Classification of Respiratory Failure”).
- Improved hemodynamics, decreased ventilator associated pneumonia, lower risk of surgical suture line damage and development of a bronchopleural fistula (see Sects. “Complications of Prolonged Intubation and Mechanical Ventilation,” and “Intrathoracic Complications”).
- Assess patient’s overall condition and search for possible etiology of new onset atrial fibrillation. Hemodynamically unstable atrial fibrillation should be treated with electrical cardioversion (see Sect. “Cardiac Complications” and Fig. 41.2).

Weaning from mechanical ventilation:

- When postoperative patients require mechanical ventilation, it is usually temporary and they should be frequently assessed for extubation.

- Evaluate respiratory rate, tidal volume, oxygen and PEEP requirements, level of consciousness, hemodynamic stability, volume status, pH and CO_2 levels, ability to cough and clear secretions, analgesia, temperature and electrolyte status (see Sect. “Classification of Respiratory Failure”).
- The rapid shallow breathing index and negative inspiratory force may help predict whether a patient will tolerate extubation. When a patient meets extubation criteria, a spontaneous breathing trial should be administered (see Sect. “Criteria for Extubation”).

Considerations with new onset atrial fibrillation:

- New onset postoperative atrial fibrillation is common after pneumonectomy.
- Patients should undergo a complete evaluation of their overall wellbeing, including a search for underlying infection, volume overload, hypoxia and hypercarbia, and electrolyte abnormalities (see Sect. “Cardiac Complications”).
- Patients who are hemodynamically stable may be managed medically with rate control, while hemodynamically unstable patients should be electrically cardioverted into sinus rhythm (Fig. 41.2).

References

1. Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G. Airway closure, atelectasis and gas exchange during general anesthesia. *Br J Anaesth.* 1998;81:681–6.
2. Hedenstierna G, Rothen HU. Atelectasis formation during anesthesia: causes and measures to prevent it. *J Clin Monit.* 2000;16:329–35.
3. MacIntyre N. Evidence-based guidelines for weaning and discontinuing ventilatory support. *Chest.* 2001;120:375S–96.
4. MacIntyre N. Discontinuing mechanical ventilatory support. *Chest.* 2007;132:1049–56.
5. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med.* 1991;324:1445–50.
6. Meade M, Guyatt G, Cook D, Griffith L, Sinuff T, Kergl C, et al. Predicting success in weaning from mechanical ventilation. *Chest.* 2001;120:400S–24.
7. Moreno P, Alvarez A, Algar FJ, Cano JR, Espinosa D, Cerezo F, et al. Incidence, management and clinical outcomes in patients with airway complications following lung transplantation. *Eur J Cardiothorac Surg.* 2008;34:1198–205.
8. Alvarez A, Algar J, Santos F, Lama R, Aranda JL, Baamonde C, et al. Airway complications after lung transplantation: a review of 151 anastomoses. *Eur J Cardiothorac Surg.* 2001;19:381–7.
9. Yap FH, Lau JY, Joynt GM, Chui PT, Chan AC, Chung SS. Early extubation after transthoracic oesophagectomy. *Hong Kong Med J.* 2003;9:98–102.
10. Lanuti M, de Delva PE, Maher A, Wright CD, Gaißert HA, Wain JC, et al. Feasibility and outcomes of an early extubation policy after esophagectomy. *Ann Thorac Surg.* 2006;82:2037–41.
11. Cordos I, Bolca C, Paleru C, Posea R, Stoica R. Sixty tracheal resections—single center experience. *Interact CardioVasc Thorac Surg.* 2009;8:62–5.

12. Almada CP, Martins FA, Tardelli MA, Tardelli MA, Amaral JL. Time of extubation and postoperative outcome after thoracotomy. *Rev Assoc Med Bras.* 2007;53:209–12.
13. Raiten J, Thiele RH, Nemergut EC. Anesthesia and intensive care management of patients with brain tumors. In: Kaye AH, Laws ER, editors. *Brain Tumors.* 3rd ed. Philadelphia: Elsevier; 2011 (in press).
14. Knoll H, Ziegeler S, Schreiber JU, Buchinger H, Bialas P, Semyonov K, et al. Airway injuries after one-lung ventilation: a comparison between double-lumen tube and endobronchial blocker. *Anesthesiology.* 2006;105:471–7.
15. Minambres E, Gonzales-Castro A, Buron J, Suberviela B, Balles-teros MA, Ortiz-Melon F. Management of postintubation tracheobronchial rupture: our experience and a review of the literature. *Eur J Emerg Med.* 2007;14:177–9.
16. Roberts J, Wadsworth J. Recurrent laryngeal nerve monitoring during mediastinoscopy: predictors of injury. *Ann Thorac Surg.* 2007;83:388–92.
17. Sagawa M, Donjo T, Isobe T, Notake S, Nakai M, Sugita M, et al. Bilateral vocal cord paralysis after lung cancer surgery with a double-lumen endotracheal tube: a life-threatening complication. *J Cardiothorac Vasc Anesth.* 2006;20:225–6.
18. Javadpour H, Sidhu P, Luke D. Bronchopleural fistula after pneumonectomy. *Ir J Med Sci.* 2003;172:13–5.
19. Hollaus PH, Setinek U, Lax F, Pridun NS. Risk factors for bronchopleural fistula after pneumonectomy: stump size does matter. *Thorac Cardiovasc Surg.* 2003;51:162–6.
20. Dentali F, Malato A, Ageno W, Imperatori A, Cajozzo M, Rotolo N, et al. Incidence of venous thromboembolism in patients undergoing thoracotomy for lung cancer. *J Thorac Cardiovasc Surg.* 2008;135:705–6.
21. Chen Q, Tang A, Tsang G. Acute pulmonary thromboembolism complicating pneumonectomy: successful operative management. *Eur J Cardiothorac Surg.* 2001;19:223–5.
22. Soll C, Hahnloser D, Frauenfelder T, Russi EW, Weder W, Kestenholz PB. The postpneumonectomy syndrome: clinical presentation and treatment. *Eur J Cardiothorac Surg.* 2009;35:319–24.
23. Shen KR, Wain JC, Wright CD, Grillo HC, Mathisen DJ. Post-pneumonectomy syndrome: surgical management and long-term results. *J Thorac Cardiovasc Surg.* 2008;135:1210–9.
24. Ng T, Ryder BA, Maziak DE, Shamji FM. Thorascopic approach for the treatment of postpneumonectomy syndrome. *Ann Thorac Surg.* 2009;88:1015–8.
25. Slinger P. Post-pneumonectomy pulmonary edema: is anesthesia to blame? *Curr Opin Anaesthesiol.* 1999;12:49–54.
26. Parquin F, Marchal M, Mehiri S, Herve P, Lescot B. Post-pneumonectomy pulmonary edema: analysis and risk factors. *Eur J Cardiothorac Surg.* 1996;10:929–32.
27. Alvarez JM, Bairstow BM, Tang C, Newman MA. Post-lung resection pulmonary edema: a case for aggressive management. *J Cardiothorac Vasc Anesth.* 1998;12:199–205.
28. Mogayzel Jr PJ, Colombani PM, Crawford TO, Yang SC. Bilateral diaphragm paralysis following lung transplantation and cardiac surgery in a 17 year old. *J Heart Lung Transplant.* 2002;21:710–2.
29. Qureshi A. Diaphragm paralysis. *Semin Respir Crit Care Med.* 2009;30:315–20.
30. Ugalde P, Miro S, Provencher S, Quevillon M, Chau L, Deslauriers DR, et al. Ipsilateral diaphragmatic motion and lung function in long-term pneumonectomy patients. *Ann Thorac Surg.* 2008;86:1745–52.
31. De Decker K, Jorens PG, Van Schil P. Cardiac complications after noncardiac thoracic surgery: an evidence-based current review. *Ann Thorac Surg.* 2003;75:1340–8.
32. Groves J, Edwards ND, Carr B, Sherry KM. Perioperative myocardial ischaemia, heart rate and arrhythmia in patients undergoing thoracotomy: an observational study. *Br J Anaesth.* 1999;83:850–4.
33. Roselli EE, Murthy SC, Rice TW, Houghtaling PL, Pierce CD, Karchmer DP, et al. Atrial fibrillation complicating lung cancer resection. *J Thorac Cardiovasc Surg.* 2005;130:438–44.
34. Diaz-Guzman E, Mireles-Cabodevila E, Arrossi A, Kanne JP, Budev M. Amiodarone pulmonary toxicity after lung transplantation. *J Heart Lung Transplant.* 2008;27:1059–63.
35. Baaijens PF, Hasenbos MA, Lacquet LK, Dekhuijzen PN. Cardiac herniation after pneumonectomy. *Acta Anaesthesiol Scand.* 1992;36:842–5.
36. Deiraniya A. Cardiac herniation following intrapericardial pneumonectomy. *Thorax.* 1974;29:545–52.
37. Shimizu J, Ishida Y, Hirano Y, Tatsuzawa Y, Kawaura Y, Nozawa A, et al. Cardiac herniation following intrapericardial pneumonectomy with partial pericardectomy for advanced lung cancer. *Ann Thorac Cardiovasc Surg.* 2003;9:68–72.
38. Buniya P, Aluffi A, Rescigno G, Rademacher J, Nazari S. Cardiac herniation and torsion after partial pericardectomy during right pneumonectomy. *Tex Heart Inst J.* 2001;28:73.
39. Zandberg FT, Verbeke SJ, Snijder RJ, Dalinghaus WH, Roeffel SM, Van Swieten HA. Sudden cardiac herniation 6 months after right pneumonectomy. *Ann Thorac Surg.* 2004;78:1095–7.
40. Bakris NC, Siddiqi AJ, Fraser Jr CD, Mehta AC. Right to left interatrial shunt after pneumonectomy. *Ann Thorac Surg.* 1997;63:198–201.
41. Zueger O, Soler M, Stulz P, Jacob A, Perruchoud AP. Dyspnea after pneumonectomy: the result of an atrial septal defect. *Ann Thorac Surg.* 1997;63:1451–2.

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Key Points

- Although pure hypoxic or pure hypercapnic respiratory failure may occur after thoracic surgery, most patients exhibit a mixed picture.
- The single most important preoperative patient-related risk factor for respiratory failure after thoracic surgery is the presence of severe COPD.
- Noninvasive ventilation (NIV) can be safely administered in the postthoracic surgery patient, both to reduce respiratory complications and to prevent the need for intubation.
- Mechanical ventilation after thoracic surgery should follow a “lung protective” strategy of appropriate combinations of PEEP and low tidal volume, in association with increased respiratory rate as needed.
- Ventilator-associated pneumonia (VAP) is associated with a high mortality, so prevention is a priority. The “VAP bundle” is a variety of care processes either known or believed to reduce the risk of acquiring VAP.
- A daily spontaneous breathing trial is the most effective way to identify patients ready for withdrawal of ventilator support.
- Tracheotomy should be considered if mechanical ventilation is expected to be required for more than a total of 7–10 days.

Introduction

Respiratory failure following thoracic surgery is a significant cause of morbidity and mortality in this high-risk patient population. The incidence of major postthoracotomy pulmonary complications such as pneumonia, lobar atelectasis, or need for mechanical ventilation for more than 24 h ranges from 22 to 25%, while the incidence of respiratory failure (requiring mechanical ventilation for more than 48 h after surgery) ranges from about 3 to 10% [1–5]. In most reports, respiratory failure accounts for approximately half of the 30-day mortality. The reported incidence of respiratory failure and overall mortality for several thoracic procedures is given in Table 42.1. Respiratory failure and mortality are greater after right-sided as compared to left-sided pneumonectomy, and after extra vs. intra-pleural pneumonectomy [6]. The addition of chest wall resection to intrathoracic surgery also adds to the incidence of respiratory failure and mortality [2]. Pre-existing pulmonary disease and other concomitant disease processes increase the risk of postoperative respiratory insufficiency and failure. Anticipation and early recognition are essential to provide the best possible outcome for the patient in respiratory failure.

TABLE 42.1. Respiratory failure^a and 30 day mortality after open^b thoracic surgery procedures.

	Respiratory failure	Overall mortality
Lung resection		
Wedge resection	Not reported	0.8–1.4% [1, 2]
Lobectomy	3.2–6.6% [3, 5]	1.2–4% [1–5]
Pneumonectomy	6.9–9.3% [3, 5]	3.2–11.5% [1–5]
Esophagogastrectomy	16% [57]	2.1–9.8% [54–57]
Lung volume reduction surgery	13.6% [48]	2.3–16% [47–50]

In two reports lobectomy was not separated from pneumonectomy: in one the incidence of tracheostomy was 14% [1]; in the other the incidence of respiratory failure was 6% [2]

^aDefined as the need for mechanical ventilation for more than 48 h after surgery

^bLimited data for thoracoscopic procedures suggests reduced overall complications but not mortality vs. open procedures [46]

Definition

Respiratory failure is the inability of the respiratory system to provide sufficient gas exchange to prevent life-threatening hypoxemia and/or hypercapnia. The clinical picture suggests the diagnosis, and the arterial blood gas (ABG) analysis is confirmatory (Table 42.2). Respiratory failure may be purely hypoxicemic, in which arterial partial pressure of oxygen in the blood is inadequate, but normal or low arterial partial pressure of carbon dioxide. Physiologic causes of hypoxicemic respiratory failure include hypoventilation, ventilation–perfusion mismatch, right-to-left intrapulmonary or intracardiac shunts, abnormalities in alveolar oxygen diffusion, and low fraction of inspired oxygen [7]. Failure to oxygenate the blood after thoracic surgery is usually the result of severe mismatch of ventilation and perfusion (“V:Q mismatch”) such that pulmonary blood flows through poorly ventilated or edematous lung and there is inadequate time or alveolar exposure for absorption of O₂. Increased pulmonary water from direct surgical injury, capillary leak, or fluid overload may cause V:Q mismatch, as may focal areas of consolidation from collections (air, blood), infection, inflammation, or atelectasis. The most severe form of V:Q mismatch is true shunting of pulmonary blood without any absorption of O₂, as might occur with a completely atelectatic or consolidated segment or lobe.

Hypoventilation alone may result in hypoxemia. The simplified form of the alveolar gas equation estimates the partial pressure of oxygen in the alveoli based on the inspired partial pressure of oxygen and the partial pressure of arterial carbon dioxide:

$$P_A O_2 = P_i O_2 - P_a CO_2 / R.$$

P_AO₂ is the alveolar partial pressure of oxygen, P_iO₂ is the partial pressure of inspired oxygen, and P_aCO₂ is the arterial partial pressure of carbon dioxide (R represents the respiratory exchange ratio). Severe hypoventilation, with a resultant rise in P_aCO₂, would therefore be expected to result in some

TABLE 42.2. Diagnosis of acute respiratory failure.

Clinical	
Central nervous system	Agitation, restlessness, diaphoresis from distress Headache, confusion from hypercarbia or hypoxemia Dizziness, focal twitching from hypercarbia Insomnia, Personality change from hypoxemia Stupor, confusion, coma from severe hypercarbia or severe hypoxemia Seizures from severe hypoxemia Tachyarrhythmias from hypoxemia or hypercarbia Bradycardia from severe hypoxemia Systemic hypertension from hypoxemia or hypercarbia Pulmonary hypertension from hypoxemia or hypercarbia Hypotension/cardiac failure from severe hypoxemia or hypercarbia Intact respiratory drive
Cardiovascular system	Tachypnea Labored respirations, dyspnea Intercostal retractions Impaired respiratory drive: bradypnea or apnea Cheyne-Stokes respirations
Respiratory system	
Laboratory	
Oxygenation ^a	Arterial pO ₂ <50–60 mmHg Peripheral arterial saturation (pulse oximetry) <90%
Carbon dioxide ^b	Arterial pCO ₂ >50–60 mmHg associated with acidosis

^aRespiratory “failure” due to hypoxemia may not require mechanical ventilatory support if it is responsive to supplemental oxygen therapy

^bChronic elevations in arterial pCO₂ are accompanied by retention of bicarbonate and relatively normal arterial pH, and do not necessarily indicate respiratory “failure.” Hypercarbia associated with acidosis always indicates respiratory failure and usually requires mechanical ventilatory support

degree of hypoxemia. The degree of hypoxemia caused by pure hypoventilation can usually be overcome by supplemental oxygen [8].

Intracardiac shunt with right- to left-sided blood flow causes arterial desaturation independent of pulmonary pathology. The condition where this most commonly occurs in the adult is a patent foramen ovale (PFO), which is present – at least in a probe-patent form – in approximately 25% of the population [9]. Short of actual closure of the shunt, the treatment requires reducing the gradient for blood flow from right to left: either reducing the right atrial pressure or increasing the left atrial pressure. In the presence of a PFO, application of increasing levels of positive intrathoracic pressure (positive end-expiratory pressure or PEEP) can worsen arterial oxygenation [10]. Positive intrathoracic pressure can increase impedance to ejection by the right ventricle, resulting in an elevation in the central venous pressure (CVP). This may increase blood flow across the atrial septum from right to left.

Hypercapnic respiratory failure occurs when ventilation of the lungs is insufficient to maintain an adequate arterial partial pressure of carbon dioxide. Hypercapnic respiratory failure may occur with structural or functional abnormalities of the chest wall and muscles of respiration. Decreased function of the muscles of respiration may be seen with residual neuromuscular blockade and with surgical disruption. Structural or mechanical problems with the chest wall induced by surgery can lead to hypoventilation by affecting the normal decrease in intrathoracic pressure seen during inspiration. These include pneumothorax, pulmonary contusion leading to decreased distensibility of the lung tissue, and flail chest. These types of hypercapnic failure are associated with respiratory distress and usually tachypnea: the patient is trying to achieve a normal arterial pCO_2 but cannot. Decreased central respiratory drive results in hypoventilation. Decreased central drive may be seen with residual anesthesia, postoperative sedation, or central nervous system disease (e.g., perioperative stroke). Conditions associated with chronic carbon dioxide retention (e.g., obstructive airways disease, obesity-hypoventilation syndrome) may be exacerbated by depressant medications or structural changes induced by surgery.

Although pure hypoxic or pure hypercapnic respiratory failure may be seen, most surgical patients with postoperative respiratory failure exhibit a mixed picture. Chest wall and parenchymal injury, edema, retained secretions or blood, and atelectasis interfere with gas exchange and increase the work of breathing. Surgical injury to the chest wall and pain also interfere with normal mechanical function, thus decreasing the effectiveness of the respiratory effort and increasing the work of breathing.

Preoperative Predictors of Respiratory Failure

Conflicting results in the available literature make establishing precise criteria for determining those patients most at risk for postoperative respiratory failure difficult. The history, physical examination, and specific investigations enable the surgeon and anesthesiologist to estimate risk and identify processes that can be treated or optimized prior to surgery. Preoperative assessment for pulmonary resection is discussed in Chap. 2. Preoperative factors associated with an increased incidence of postoperative respiratory failure are summarized in Table 42.3.

History

Preexisting conditions which have been associated with increased risk of respiratory dysfunction and failure in the general surgery patient population include advanced age (greater than 70 years), chronic pulmonary disease, smoking, cardiac dysfunction, and neuromuscular diseases affecting the muscles of respiration or glutition [11]. Arozullah et al.

TABLE 42.3. Preoperative factors associated with increased risk of postoperative respiratory failure.

History
Age >70 years
Smoking history with chronic obstructive pulmonary disease
Cardiac dysfunction
Neuromuscular disease
Dyspnea at rest or with light exertion
Inability to climb 1 flight of stairs
Physical findings
Increased baseline work of breathing
Preoperative wheezing (not controlled by bronchodilators)
Lower extremity edema/jugular venous distension (suggestive of right heart dysfunction)
Cachexia
Laboratory
$\text{pCO}_2 >45 \text{ mmHg}$
$\text{pO}_2 <50 \text{ mmHg}$ on room air
$\text{ppoFEV}_1 <40\%$ predicted
$\text{ppoDLCO} <40\%$ predicted
$\text{RV/TLC} >30\%$
$\text{VO}_2 \text{ max} <15 \text{ mL/kg/min}$
Increased serum creatinine

ppo predicted postoperative; *DLCO* diffusion capacity for carbon monoxide; *FEV*₁ forced expiratory volume in 1 s; *RV* residual volume; *TLC* total lung capacity; *VO*₂ *max* maximum oxygen consumption

published a multifactorial index for predicting postoperative respiratory failure which includes chronic obstructive pulmonary disease (COPD), increased age, dependent functional status, and surgical site as independent risk factors for patients in the general surgical population [12]. Patients who report dyspnea at rest, with light exercise (walking on a level surface 100 yards), or with activities of daily living (dressing, talking) have an approximate twofold increase in respiratory complications following thoracotomy [13]. In a recent review from the Cleveland Clinic, preoperative predictors of postoperative ventilator support after thoracotomy for lung resection included elevated creatinine and low preoperative forced expiratory volume in 1 s (FEV₁) [14].

The single most important preoperative patient-related risk factor is the presence of COPD, and the incidence of postoperative pulmonary complications associated with COPD increases with the severity of the disease. The relative risk of pulmonary complications in patients with COPD is three to fourfold [15]. These patients should have management of their airway obstruction optimized prior to surgery with a multimodal approach consisting of bronchodilators, smoking cessation, antibiotics, and corticosteroids.

Asymptomatic asthma is not associated with any increase in the incidence of pulmonary complications or need for postoperative mechanical ventilation after thoracotomy. If the patient is free of wheezing in the immediate preoperative period and the FEV₁ is greater than 80% predicted, there is no increased risk of bronchospasm or other pulmonary complications [16]. On the other hand, an asthmatic patient with recent episodes of bronchospasm and wheezing should be treated

cautiously. These patients may benefit from prophylactic corticosteroid use before anesthesia and surgery. The Global Initiative for Asthma (GINA) guidelines state: “If FEV_1 values are less than 80% of the patient’s personal best, a brief course of glucocorticosteroids is required to reduce airflow limitation” [17]. Steroids may be administered orally or by inhalation with inhaled steroids leading to less systemic side effects. Patients who have recently had significant asthma symptoms and received systemic glucocorticosteroids within the past 6 months should have systemic coverage during the perioperative period. All asthmatic patients should remain on their routine bronchodilator and anti-inflammatory medications in the perioperative period. Perioperative nutrition is also important in these patients [18].

Procedure and Extent of Resection

Thoracotomy for Lung Resection

The extent of resection during thoracotomy for lung cancer is a risk factor for the need for postoperative mechanical ventilation, pulmonary complications, and 30-day mortality (Table 42.1) [14]. In addition, Busch et al. reported an 82% incidence of postoperative pulmonary complications in patients requiring extensive resection, including the chest wall. This compared to an overall incidence of 39% in their study of patients undergoing thoracotomy [2]. On the other hand, a review of the muscle-sparing thoracotomy approach (where the latissimus dorsi and serratus anterior muscles are not severed) vs. standard thoracotomy found no morbidity or mortality benefit [19]. Not surprisingly, older studies and more recent reports have found increasing age to be a major risk factor for the development of serious pulmonary complications including respiratory failure and mortality [4, 5, 20].

Video Video-Assisted Thoracic Surgery for Lung Resection

Minimally invasive lung surgery has gained popularity because of the smaller incision, potentially shorter hospital stay, and quicker recovery (see also Chap. 23). Video-assisted thoracic surgery (VATS) is performed through several small ports rather than a single long incision, resulting in less interference with pulmonary mechanics, decreased postoperative pain, and possibly less morbidity and mortality. Imperatori et al. reported a reduced incidence of prolonged air leak and pneumonia; other postoperative pulmonary complications were not reported [21]. Although some studies support better outcomes compared to thoracotomy, limited evidence supports the theory that VATS for lobectomy improves long-term outcomes [22, 23]. Also, concern still exists that the extent of the resection may be inadequate in certain patient populations [22]. The reality is that many surgeons are performing VATS and many patients are requesting it.

Lung Volume Reduction Surgery

Lung volume reduction is a surgical strategy to improve ventilation–perfusion matching in patients with severe emphysema (see also Chap. 36). Prospective candidates usually have a FEV_1 of less than 30% predicted and poor exercise tolerance secondary to dyspnea. During lung volume reduction surgery, nonfunctional portions of lung are removed (up to 30% of lung volume in some patients). The goal is improvement of chest wall mechanics and elastic recoil of lung by removing poorly ventilated and perfused apical segments [24]. Surgery in these very high-risk patients does carry a significant risk of postoperative respiratory complications. In one report the incidence of postoperative acute respiratory failure was 29.8%, with 43% of mortality related to a respiratory etiology [25]. Overall, the reported mortality following lung volume reduction surgery ranges from a low of 2.3% to up to 16% [26, 27].

Transsternal Thymectomy

Thymectomy is performed in patients with myasthenia gravis who have worsening symptoms despite maximal medical therapy with anticholinesterase medications and/or corticosteroids, and has been shown to improve symptoms in up to 75% of patients (see also Chap. 15) [28]. In the perioperative period, the myasthenic patient may show exquisite sensitivity to nondepolarizing neuromuscular blocking medications, and may have increased sensitivity to medications with respiratory depression side effects. In the past these patients remained intubated after surgery, and were only extubated after careful assessment and reinstitution of preoperative anticholinesterase medications. As medical management has improved many of these patients now present for surgery with their disease well controlled, and with careful anesthetic management can be extubated immediately after the procedure. Historically, preoperative predictors of the need for postoperative ventilatory support include duration of the disease greater than 6 years, chronic lung disease, a daily dose of pyridostigmine greater than 750 mg (or its equivalent), and a preoperative vital capacity less than 2.9 L [29]. In a series of 71 patients undergoing thymoma resection, the incidence of postoperative respiratory complications was 13%, with only one death due to respiratory failure [30]. An increasing use of thoracoscopic techniques for this procedure may reduce the incidence of postoperative respiratory complications.

Esophagogastrectomy

The incidence of adenocarcinoma of the distal esophagus has increased over the last several decades, with risk factors including a history of tobacco use and alcohol consumption [31]. Esophagogastrectomy offers the only hope of cure.

Esophagogastrectomy for carcinoma at or near the gastroesophageal junction may be performed via a transhiatal approach or via a transthoracic approach (see also Chap. 30). Pulmonary complications occur in 15–25% of patients, with pneumonia and/or respiratory failure comprising about half of this

incidence. The in-hospital mortality rate following transthoracic esophagogastrectomy ranges from 2.1 to 9.8% [32–34]. Two of three postesophagectomy mortalities are related to pulmonary complications; aspiration pneumonia secondary to postoperative swallowing disorders is the most common etiology [35].

Lung Transplantation

Lung transplantation is increasingly performed for end-stage lung disease secondary to many etiologies, limited to a large degree by donor availability. Following reperfusion of the donor lung, more than half the patients exhibit some degree of noncardiogenic pulmonary edema, and postoperative mechanical ventilation for at least 24 h is normal. This is discussed below under “pulmonary edema.”

Thoracoabdominal Aortic Aneurysm (TAAA) Repair

The most common complications after open TAAA repair are pulmonary. These procedures require extensive incisions, prolonged periods of one-lung ventilation, and large volume fluid resuscitation. Reporting on 100 consecutive TAAA repairs, Money et al. found the mean duration of intubation to be 5.8 days, with a 21% incidence of respiratory failure [36]. An earlier report from Crawford’s group suggested an incidence of respiratory failure in patients with chronic pulmonary disease of 58% and a mortality of 43% in this group [37]. Etz et al. recently reported an incidence of prolonged respiratory failure of 27% [38].

Specific Causes of Respiratory Failure

Table 42.4 summarizes the common conditions leading to acute postoperative respiratory failure. Similar to the diagnosis itself, the cause is seldom single or simple; more often it represents the combination of postoperative factors with predisposing physiology or underlying conditions.

TABLE 42.4. Acute causes of respiratory failure following thoracic surgery.

Atelectasis/retained secretions
Pneumonia
Pulmonary embolus
Pulmonary edema
Postpneumonectomy pulmonary edema
Pulmonary reimplantation response
Acute respiratory distress syndrome
Pneumothorax
Bronchopulmonary fistula
Torsion of residual lobe
Neurologic injuries
Phrenic nerve
Recurrent laryngeal nerves

Atelectasis

Surgery on the thorax and the upper abdomen leads to some degree of postoperative pulmonary dysfunction and atelectasis, which may persist for days or weeks. Inhibition of surfactant, gas resorption, and compression of lung tissue all are potential mechanisms by which atelectasis occurs. Although general anesthesia has been shown to depress the function of surfactant, inhibition of surfactant is not believed to play a major role in the formation of atelectasis [39, 40]. Resorption atelectasis refers to the continued gas uptake in alveoli after airway occlusion and ultimately leads to collapse of the gas pocket [41]. Resorption atelectasis increases with increasing inspired oxygen concentration [42]. Lastly, loss of intercostal muscle tone and cephalad displacement of the diaphragm and abdominal contents leads to an increase in pleural pressures and compression atelectasis [43].

The relationship between functional residual capacity (FRC) and closing capacity (CC) must also be considered. FRC is defined as the amount of air remaining in the lung at end expiration of a normal tidal volume. CC is the volume of gas that must be in the lungs to prevent small airway collapse. In healthy lungs, FRC exceeds CC and no atelectasis occurs. If CC exceeds FRC and the tidal volume lies within the CC, then small airways will open and close with each tidal volume. This will result in areas of low ventilation/perfusion ratio or shunt. If CC far exceeds FRC, then small airways never open during the respiratory cycle and results in atelectasis (Fig. 42.1). Thus, factors that decrease FRC like general

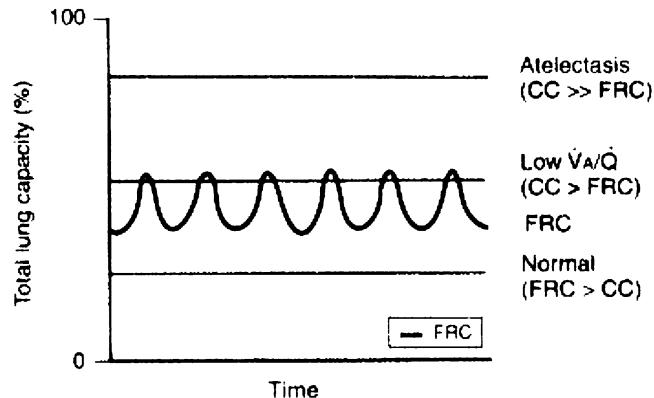


FIG. 42.1. Closing capacity (CC): The relationship between the functional residual capacity (FRC) and CC. FRC is the amount of gas in the lungs at end-exhalation during normal tidal breathing, shown by the level of each trough of the sine wave of normal tidal volume. CC is the amount of gas which needs to remain in the lung to keep the small conducting airways open. The figure shows three different CCs indicated by the three horizontal lines. If tidal ventilation occurs such that FRC is above a normal CC (lowest horizontal line) this will preserve best gas exchange. If the CC is high (highest horizontal line) or FRC is low, tidal ventilation may occur with part of the lung atelectatic, resulting in hypoxemia. If tidal ventilation occurs at a lung volume near the CC (middle line) or FRC then there will be increased V/Q mismatch, also resulting in hypoxemia (this article was published in [172]).

TABLE 42.5. Adjuvants to routine post-operative respiratory care.

Inhaled bronchodilators and mucolytics
Incentive spirometry
Positive expiratory pressure valves
Flutter valves
Chest physiotherapy
Percussion/vibration
Nasotracheal suctioning
Fiberoptic bronchoscopy
Therapeutic
Diagnostic
Minitracheostomy

anesthesia, obesity, and supine position will subject patients to atelectasis.

While some degree of atelectasis occurs in almost all post-thoracotomy patients, the severity and clinical implications vary widely. Mild atelectasis usually requires little treatment other than supplemental oxygen administration in the post-anesthesia care unit (PACU) and will resolve as the patient awakens and increases depth of breathing. Decreased compliance, impaired oxygenation, increased pulmonary vascular resistance, and development of lung injury represent the more severe pathophysiologic effects of atelectasis. The most severe form of postlobectomy atelectasis, lobar atelectasis, occurs in approximately five percent of patients after pulmonary resection. Lobar atelectasis is defined roentgenographically by complete lobar collapse and mediastinal shift. Risk factors include male gender, advanced age, and reduced preoperative FEV₁ [43]. This extreme form of atelectasis usually requires bronchoscopy, may require mechanical ventilatory support, and can lead to longer intensive care unit (ICU) and hospital lengths of stay. Lastly, atelectasis has been shown to promote bacterial overgrowth and increase lung permeability [44].

Prevention and treatment of atelectasis has traditionally consisted of cough and deep breathing exercises (Table 42.5). While coughing and deep breathing help clear secretions and potentially reopen atelectatic areas of lung, the ability of surgical patients to cough is significantly impaired after thoracic surgery. The maximal intrapleural pressures produced during voluntary coughing are reduced to as low as 29% of preoperative values, and may remain as low as 50% of the preoperative value at 3 weeks postsurgery [45]. The cough effort may be improved with the patient in the sitting position and with manually assisted compression of the chest wall. Simply mobilizing patients from sitting in bed to sitting in a chair improved FRC an average of 17% [46].

Incentive spirometry (IS) is a simple and inexpensive method of helping patients obtain maximal inspiratory effort [47]. IS encourages patients to maintain inspiration for a prolonged period while using slow and deep breaths. Figure 42.2 shows a typical single-patient use IS device. IS can also be followed as a bedside test for evaluation of postoperative pulmonary function after lung surgery. The performance on IS correlates well with inspiratory reserve volume and forced



FIG. 42.2. Incentive spirometer (Hudson RCI, Teleflex Medical): The patient makes a sustained inhalation effort through the mouthpiece, guided by an effort indicator on the right side of the device. This causes the “floating” marker inside the graduated cylinder to be drawn up to a set target indicated to the left of the cylinder.

vital capacity [48]. A decline in a patient’s ability to perform IS can be an early indicator of an acute worsening of the patient’s pulmonary status. While IS is widely accepted as a tool to help prevent atelectasis, this has not been clearly established in clinical studies. Several reviews of the literature have failed to find supporting evidence for the routine use of IS following cardiac, thoracic, or upper abdominal surgery [49–52].

An alternative approach to IS is to focus on maintaining airway patency during expiration. This is termed “positive expiratory pressure therapy” (PEP) and has been shown to improve clearance of secretions [53] (Fig. 42.3). The patient uses this device for several breaths, and then makes coughing or “huffing” efforts. Yet a third type of device is the “flutter valve” which causes “fluttering” of the expiratory airway pressure, aiding the mobilization of secretions.

Positive pressure breathing (i.e., positive inspiratory pressure) through a mouthpiece or facemask, or continuous positive airway pressure (CPAP; see description in “ventilatory modes”) delivered by nasal or facemask may be beneficial in maintaining and recruiting atelectatic lung [54]. Biphasic, or bilevel, positive airway pressure (BiPAP) has also been used to support hypoxic patients in the PACU [55]. Figure 42.4 illustrates the nasal mask used for BiPAP or CPAP. The role of nasal BiPAP in prevention or treatment of acute respiratory failure is discussed later.

Pain is a major factor contributing to the reduction in cough effort and deep breathing in patients following thoracotomy. Adequate control of postoperative pain, including use of epidural analgesia, improves maximal cough pressures in post-thoracotomy patients, and lack of a thoracic epidural catheter



FIG. 42.3. Positive expiratory pressure vibratory device (“Acapella” device, Smiths Medical ASD, Inc.): exhalation through this device is intermittently occluded at a high frequency which “vibrates” the airways facilitating clearance of secretions and possibly opening closed airways.



FIG. 42.4. Long tube changer for use with double-lumen tracheal tubes (Cook Medical): a double-lumen tube is illustrated with the tube changer curved around it; the tube changer is more than twice the length of the double-lumen tube.

was found to be a risk factor for the need for postoperative mechanical ventilation after lung resection [14, 56]. While the use of opioid infusions through either lumbar- or thoracic-level epidural catheters can provide adequate postthoracotomy analgesia, only analgesia provided by thoracic-level catheters was demonstrated to decrease mortality in a recent meta-analysis of postoperative outcomes [57]. Various infusions may be used including an opioid alone or, for a thoracic level catheter, an opioid and local anesthetic combination. The combination of an opioid and local anesthetic has been shown to be synergistic and allows for a lower dose of each than if either is used alone [58]. A technique gaining popularity for thoracic patients is a continuous paravertebral catheter. This technique offers the advantages of fewer side effects compared to a thoracic

epidural and is not contraindicated in anticoagulated patients. A literature review by Davies indicates that continuous paravertebral catheters are just as efficacious in pain control as thoracic epidurals [59]. Other modalities of regional anesthesia to provide postthoracotomy analgesia include intrapleural administration of local anesthetic and intercostal nerve blocks. Intercostal nerve blocks may be performed by the anesthesiologist pre- or postoperatively or by the surgeon during the procedure. The blocks may be performed with local anesthetic or, for a more protracted duration of analgesia, phenol. Intraoperative cryoablation of intercostal nerves has also been used to provide an extended period of analgesia.

Bronchospasm

In patients with known bronchospastic disease, or in patients with COPD shown to have improvement after bronchodilators during preoperative spirometry, postoperative airway constriction may contribute to respiratory failure. Increased airway resistance contributes to increased work of breathing, and also can create the “auto-PEEP” effect. This occurs when terminal bronchioles/alveoli do not fully empty through narrowed airways during expiration, resulting in a positive rather than zero pressure at end-expiration distal to the obstruction. In order to generate flow into these alveoli during inspiration, this positive pressure must first be overcome, creating a further increase in the work of breathing [60].

Inhaled bronchodilating agents should be considered in all patients exhibiting respiratory distress after thoracic surgery. Inhaled beta-adrenergic agonists enhance smooth muscle relaxation by increasing intracellular levels of cyclic AMP and ultimately results in bronchodilation [61]. Inhaled albuterol is the beta-adrenergic agonist most often prescribed in the postoperative period due to its short onset time and ability to act as a rescue medication. The half-life of albuterol is short and requires dosing every 4 h. Salmeterol and Formoterol are longer acting beta-adrenergic agonist and are mainly used as maintenance therapy [62]. Racemic epinephrine also has beta-adrenergic properties and may reduce respiratory mucosal edema through its alpha-adrenergic effects on mucosal vasculature. A concern with these agents, especially epinephrine, is absorption and systemic side effects.

Anticholinergic medications are also effective bronchodilators. These medications induce smooth muscle relaxation by antagonism of acetylcholine at the M3 receptor and decrease intracellular levels of cyclic-GMP. Ipratropium is a short onset and short duration anticholinergic medication commonly used in combination with albuterol for bronchospastic disease. Like albuterol, it needs to be dosed approximately every 4 h. Tiotropium is a longer acting anticholinergic medication that can be used for maintenance. These medications are poorly absorbed and have limited systemic side effects.

Combination therapy with a beta-adrenergic agonist and anticholinergic medication provides greater improvement in symptoms. By having different mechanism of action and

durations, these medications work synergistically to improve bronchodilation [63]. A combination of the short acting beta-adrenergic agonist albuterol and short acting anticholinergic ipratropium is available in the United States.

Lastly, steroid compounds are also available for inhalational administration and serve a useful role in prevention of inflammatory mediated bronchospasm. These medications are mainly used in maintenance therapy and are not indicated for acute bronchospasm.

Retained Secretions

Inability to clear secretions contributes to atelectasis and pulmonary infections.

Dehydration of the tracheobronchial mucosa occurs with use of nonhumidified oxygen. This leads to mucociliary dysfunction and drying of secretions. The ensuing decrease in ability to mobilize and clear secretions can contribute to the formation of atelectasis; humidification of oxygen is therefore recommended. Patients with tenacious secretions may benefit from inhaled agents that decrease the viscosity of secretions such as *N*-acetylcysteine or dornase alfa (Pulmozyme®, Genetech, Inc.). Dornase is a recombinant human DNase, which has been demonstrated to decrease viscosity of respiratory secretions in cystic fibrosis patients, and help re-expand atelectatic lobes in this population [64]. Efficacy in patients with chronic bronchitis has not been demonstrated for long-term use but has been suggested in acute exacerbations.

For the patient who fails to respond to deep breathing exercises, IS, and PEP therapy, along with inhaled bronchodilators and/or mucolytics, there are several adjuvant therapies that may be utilized to improve the patient's status (Table 42.5). Modalities of chest physiotherapy include postural drainage, percussion and vibration over the affected lung segments, and incentive to cough. Postural drainage is performed by positioning the patient so the lung segments to be drained are in a superior position. Drainage is most effective when combined with percussion and vibration but proper positioning may be limited by the patient's condition. Percussion is performed throughout the respiratory cycle and is followed by vibration during the exhalation phase.

Tracheal suctioning can be used to mechanically remove secretions from the trachea and to induce deep breathing and coughing. In the nonintubated patient, tracheal suctioning is usually performed by a blind nasal technique. Suctioning should be performed after preoxygenating the patient with a high FiO_2 , and may be better tolerated through a nasal airway or "trumpet." The catheter should be advanced without suction and removed from the trachea with intermittent suction. Frequent or aggressive suctioning can cause mucosal damage and may induce bronchospasm, laryngospasm, and cardiac rhythm disturbances.

An alternative to blind nasotracheal suctioning is placement of a minitracheotomy (a small, uncuffed endotracheal tube through an incision in the cricothyroid membrane) to facilitate

suctioning of secretions. This procedure is safe and effective in decreasing the need for other interventions such as chest physiotherapy. This procedure also may decrease postoperative respiratory complications [65–67]. Potential complications are rare, including bleeding into the trachea, infection, and tracheal occlusion by granuloma formation [68]. Minitracheotomy is not intended to provide a means for positive pressure ventilation and is not a replacement for endotracheal intubation when indicated.

Fiberoptic bronchoscopy (FOB) may be used for more aggressive clearance of secretions or blood in the tracheobronchial tree or as a diagnostic study in the patient with an acute worsening of respiratory function. Under direct visualization, tenacious secretions can be suctioned from affected airways. A review of the practice of FOB in a large teaching hospital confirmed the safety of the procedure with a major complication rate of 0.5% and a minor complication rate of 0.8% [69]. Complications include laryngospasm, bronchospasm, pneumothorax, and pulmonary hemorrhage. In the awake, nonintubated patient, FOB requires topical anesthesia of the upper airway and sedation.

Pneumonia

Decreased mucociliary clearance and persistent atelectasis place the thoracic surgical patient at increased risk for postoperative nosocomial pneumonia. Following thoracotomy, patients also have altered systemic and lung host defenses which increase susceptibility to postoperative pneumonia [70]. The occurrence of pneumonia, especially after lung resection, significantly increases the patient's risk for respiratory insufficiency and need for mechanical ventilation. Nosocomial pneumonia is the single most important risk factor for mortality in the postthoracotomy patient [4]. In a prospective trial, Nan found the rate of postoperative respiratory infections after lung surgery (pneumonia, empyema) to be ~19% [71]. Overall, mortality rates for nosocomial pneumonia range from 20 to 80% with Gram negative bacilli and *Staphylococcus aureus* being the most common pathogens [72]. Ventilator-associated pneumonia is discussed later.

Initiation of therapy should not be delayed for the results of initial cultures. Mortality is reduced with appropriate empiric antibiotic therapy vs. delaying until bronchoalveolar lavage (BAL) is performed [73]. For suspected pneumonia occurring early in the postoperative period in a patient who was not in the hospital preoperatively, community-acquired organisms such as *Streptococcus pneumonia* and *Hemophilus influenza* should be targeted. For a patient who has been in the hospital preoperatively, or in whom pneumonia is suspected more than 48 h after surgery, empiric antibiotic therapy should target hospital-acquired organisms such as *Pseudomonas aeruginosa*, *Acinetobacter* and *Klebsiella* species, and methicillin resistant *S. aureus*. The importance of initial appropriate empiric antibiotic therapy cannot be understated, and should be targeted to institution or community specific pathogens.

Inappropriate antibiotic therapy, even if corrected within 48 h when the results of culture become available, has been associated with higher mortality, a longer ICU stay, and a trend towards longer mechanical ventilation. Inappropriate initial antibiotic therapy has been reported to be as high as 50% [73]. Ventilator-associated pneumonia is discussed later.

Pulmonary Embolism

In a study of 77 patients undergoing thoracotomy before the use of subcutaneous heparin prophylaxis, the incidence of deep venous thrombosis was 19%, with pulmonary embolism occurring in 5% [74]. In a large series of 1,735 lung resection patients, early fatal acute cardiopulmonary failure occurred in 26 patients. Autopsy in 20 of these patients demonstrated pulmonary embolism in 19 [75]. In patients with shock due to massive pulmonary emboli, the mortality is in excess of 30% [76]. As thoracic surgery patients usually have at least two major risk factors for deep venous thrombosis (malignancy and major surgery), prophylaxis should include both sequential compression devices applied to the calves, and low-dose subcutaneous heparin or low molecular weight heparin.

Signs and symptoms of pulmonary embolism include dyspnea, tachypnea, arterial hypoxemia, pulmonary hypertension, right ventricular failure, and shock. Lung perfusion scanning with technetium 99m-labeled albumin combined with ventilation scanning with xenon 133 can demonstrate areas of ventilation-perfusion mismatch, although this test is of limited use when there is preexisting lung disease or recent lung surgery. Current use of lung perfusion scanning is only in patients with renal insufficiency, anaphylaxis to intravenous contrast, or pregnancy [77]. Spiral computed tomography (CT) can demonstrate pulmonary emboli and is noninvasive, quicker, and easier to perform than ventilation-perfusion scanning [78, 79]. While the gold standard for detection of pulmonary emboli is pulmonary angiography, in many centers spiral CT has essentially eliminated the need for this more invasive test. Postoperative patients are not candidates for thrombolytic therapy, but therapeutic heparinization is usually safe if initiated at least 24–48 h after surgery. Massive embolism may require surgical embolectomy.

Pulmonary Edema

The etiology of pulmonary edema after thoracic surgery may be cardiogenic or noncardiogenic. Increased hydrostatic pressure in the pulmonary vasculature, as might be associated with left ventricular dysfunction or excessive intravenous fluid administration may lead to cardiogenic pulmonary edema. Increased permeability of the alveolar capillary membranes, as occurs with the acute respiratory distress syndrome (ARDS), leads to noncardiogenic pulmonary edema.

Postpneumonectomy pulmonary edema (PPE) is a particularly severe form of pulmonary edema that can occur after pneumonectomy and is associated with a high mortality.

Resection of lesser amounts of lung tissue (i.e., wedge resection) is not associated with this entity [80]. Patients with PPE develop a low-pressure, high-protein pulmonary edema indicating endothelial damage is present [81]. An increase in endothelial permeability has been demonstrated by measuring the pulmonary accumulation of intravenously administered technetium 99m-labeled albumin after pneumonectomy [82].

The etiology of PPE remains unclear, but is likely multifactorial. Risk factors that have been associated with PPE include the side of operation, with right pneumonectomy having a higher risk than left, perioperative fluid overload (>2 L intravenous fluid administration), and higher tidal volumes during one-lung ventilation (10 mL/kg) [83–85]. Other potential etiologies include the use of fresh frozen plasma intraoperatively, oxygen toxicity, serum cytokines, and mediastinal lymphatic damage.

The development of pulmonary edema after lung transplantation has been termed the pulmonary re-implantation response (PRR). The etiology of PRR is likely multifactorial and includes reperfusion injury, oxygen toxicity, and excess fluid administration. Although PRR has not been shown to affect survival of transplant patients, its occurrence does cause increased duration of ventilator support and ICU stay. Contrary to what might be expected, Khan et al. were not able to demonstrate that prolonged ischemic time of the donor lung or presence of pulmonary hypertension was independently associated with the development of PRR [86]. The use of cardiopulmonary bypass during the transplant procedure was shown to be an independent risk factor, however. Treatment has been primarily supportive but recently researchers have been focusing on treatment modalities that may decrease the injury caused to the donor lung by reperfusion. Inhibition of adherence of polymorphonuclear leukocytes to activated endothelium by blocking L- and E-selectins by specific antibodies demonstrated a reduced incidence of PRR in a sheep model [87]. Daclizumab, an interleukin-2 antagonist, demonstrated no significant differences in immediate clinical or radiographic manifestations of PRR, however [88]. Recent work has investigated the role of adenosine A2A receptor activation in protection from ischemia-reperfusion injury [89].

Pneumothorax

Following thoracotomy the surgeon usually places two chest tubes into the operative hemithorax. One chest tube is placed inferiorly to preferentially drain blood and fluids and a second tube superiorly to preferentially vent air. Pneumothorax may develop postoperatively if a chest tube is inadvertently kinked, clamped off, or dislodged. While a small leak may cause little or no symptoms, a large, undrained air leak can result in a “tension pneumothorax” with a shift of the trachea and mediastinum to the contralateral side. The increase in intrathoracic pressure causes a decrease in venous return to the right heart and can result in cardiovascular collapse. Pneumothorax may also occur on the nonoperative side as result of rupture of a

pulmonary cyst or bulla if excessive airway pressures develop during mechanical (especially one-lung) ventilation. Inadvertent and unrecognized surgical entry into the pleura of the non-operative side may cause pneumothorax, as may inadvertent lung puncture during placement of central venous catheters, or intrapleural catheters for postoperative analgesia.

Definitive treatment of a pneumothorax is placement of a chest tube, usually in the fourth or fifth intercostal space between the anterior and mid-axillary lines. In the case of tension pneumothorax, a needle thoracostomy is performed by placing a large-bore, i.e., 14 gauge, venous catheter above the third rib in the mid-clavicular line. This effectively converts the tension pneumothorax to a simple pneumothorax.

Persistent Air Leaks and Bronchopleural Fistula

Persistent air leaks are reported to occur in 4–20% of pulmonary resections, prolonging and complicating the postoperative course [90]. Bronchopleural fistula is associated with a large air leak from the lung and results from disruption of a bronchial stump or tracheobronchial anastomosis. The initial sign is often a dramatic increase in air leak noticed in the chest tube drainage chamber. If the air leak exceeds the capacity of the chest tube to evacuate the air, there will be a persistent pneumothorax. In large bronchopleural fistulas, respiratory insufficiency may ensue. Positive pressure ventilation poses a significant problem as the majority of tidal volume escapes into the pleural space and chest tube through the lower resistance bronchopleural fistula. Pneumonectomy, residual tumor in the bronchial stump, hyperglycemia, hypoalbuminemia, postoperative mechanical ventilation, preoperative steroid use, COPD, and low predicted postoperative FEV_1 have all been reported as risk factors for the development of bronchopleural fistulas [91].

Although definitive treatment of large leaks requires surgical correction, temporary ventilator management may include placement of a double-lumen endotracheal tube to allow differential lung ventilation (see below). Alternatively, a bronchial blocker may be used on the affected side to limit flow to that side. Smaller air leaks may be treated with endobronchial substances or devices; a recent publication describes 40 patients treated with endobronchial valves, placed via bronchoscopy [92].

Aspiration of Gastric Contents

In the thoracic surgery population, the risk of aspiration of gastric contents is increased in patients presenting with esophageal disease. Intraoperative aspiration will lead to a pulmonary injury causing edema and inflammation, leading to hypoxemia. Aspiration pneumonitis is one of the causes of ARDS, the management of which is discussed later. Not well recognized is the risk of a relatively small-volume aspiration in patients extubated after more than 48 h after thoracic surgery in general, and in particular after lung transplantation [93].

In the latter population, a study utilizing fiberoptic endoscopy demonstrated aspiration in the majority of single- and double-lung transplantation patients [94]. These patients should be evaluated for swallowing competence and risk of aspiration before oral intake is initiated postoperatively, and be watched closely for signs of aspiration.

Torsion of Residual Lobe

Torsion of a residual lobe of the lung around its bronchus may complicate lobectomy. The loss of lung tissue on the surgical side may allow abnormal movement of the residual lung tissue, most commonly the right middle lobe and the lingula. In addition to the intrapulmonary shunt that develops secondary to occlusion of the affected bronchus, blood supply to the affected lobe is compromised and can lead to infarction.

The diagnosis can be suspected by the onset of respiratory distress or failure in association with the appearance of a collapsed or abnormal lobe on the chest radiograph, which does not respond to the usual therapies for atelectasis. The diagnosis can then be confirmed by bronchoscopy. Definitive therapy consists of surgical correction of the torsion, which should be performed urgently if infarction of the lobe is to be prevented.

Neurologic Injuries

While rare following thoracic surgery, neurologic injuries may occur which can lead to pulmonary insufficiency in the postoperative period. Damage to a phrenic nerve can occur following thoracotomy, especially if extensive dissection into the mediastinum is necessary to remove a tumor. Unilateral phrenic nerve palsy is usually tolerated by a patient with good pulmonary reserve. In a patient with baseline compromised pulmonary status, such as advanced COPD, unilateral phrenic nerve paralysis will lead to difficulty in weaning from mechanical ventilation. Bilateral phrenic nerve paralysis will lead to pulmonary insufficiency in any patient. The diagnosis is suggested by elevated hemidiaphragm on postoperative chest film. It can be confirmed by observing paradoxical motion of the affected hemidiaphragm under fluoroscopy.

Recurrent laryngeal nerve injury may be seen following extensive hilar lymph node dissection. The left recurrent laryngeal nerve is at greater risk of injury due to its more caudal course. Unilateral injury is generally well tolerated but bilateral injury can cause significant stridor following extubation secondary to spasm of the vocal cord adductor muscles.

Mechanical Ventilation After Thoracic Surgery

Table 42.6 summarizes the common reasons to continue mechanical ventilation into the postoperative period after thoracic surgery. Many of these relative indications are common to major surgery of all types, and reflect planning

TABLE 42.6. Relative indications for mechanical ventilation after thoracic surgery.

Preoperative
Preoperative mechanical ventilation
Predicted low postoperative FEV ₁ (<30% predicted)
Esophagogastrectomy or thoracoabdominal aneurysm repair
Intraoperative
Prolonged intraoperative course
Massive fluid administration or transfusion
Hypothermia
Cardiac failure
Surgical complication
Need for postoperative lung isolation (air leak, drainage)
Need for postoperative chest wall immobilization/stabilization
Immediate postoperative
Incomplete recovery of neuromuscular function
Inadequate respiratory drive (excessive opioid administration)
Requirement for $\geq 50\%$ FiO ₂
Visible respiratory distress

to “stabilize” a patient after major stress. Preoperative and intraoperative discussion with the surgical team allow for appropriate arrangements to be made in advance regarding care in the “PACU” or ICU.

Two major issues in early postoperative mechanical ventilation after thoracic surgery are (1) concern for bronchial anastomoses after lung resection, and (2) leaving tracheal tubes that are designed for intraoperative lung isolation. Regarding bronchial anastomoses, there is always a concern that positive airway pressures may expose the patient to increased risk of bronchial anastomotic leaks or disruption. This must be balanced with the need for oxygenation (which may require PEEP), and adequate minute ventilation for elimination of CO₂. The clinical goal is to avoid elevated airway pressures by reducing the delivered tidal volume or by using pressure limited modes of ventilation where possible (see below). There are no publications defining the “safe” upper limit of positive airway pressure after lung resection; however, common sense dictates that lower airway pressures are safer.

Double-lumen or specialty tubes which incorporate a bronchial blocker have small inner diameters related to their outer diameter, making tracheal/airway toilet difficult and imposing additional work of breathing when this is demanded of the patient. In addition, PACU and ICU nurses, and respiratory therapists are usually unfamiliar with such tubes. Unless there is a need to continue lung isolation postoperatively (e.g., persistent large air leak, draining infection) it is desirable to replace such specialty tubes with single-lumen tubes before leaving the operating room. In those patients with difficult airways or those who have/are expected to have oral or airway edema, clinical judgment must be used; the above mentioned problems may be a necessary evil in the face of potential loss of the airway. While long tube exchanging devices for double lumen tubes are available (Fig. 42.4), use of these does not guarantee the ability to re-advance a single-lumen tube through a very edematous or difficult airway. It may be prudent to plan to change the tube at a later time/date.

Preoperative Indications for Postoperative Mechanical Ventilation

Patients coming to the operating room already ventilated for any reason are unlikely to tolerate extubation immediately after their procedure. Withdrawal of mechanical ventilation should be done in a gradual, controlled manner, and the operating room is not a suitable place for this process. Patients with poor predicted postoperative FEV₁ (less than 30% predicted) are at the highest risk for immediate postoperative respiratory failure (see Chap. 2). These patients may benefit from a staged withdrawal of mechanical ventilation while other physiology is assured to be optimal (cardiac, endocrine, renal) and normothermia and analgesia are achieved. Specific major procedures that are usually associated with *elective* postoperative mechanical ventilation for at least 24 h include esophagectomy or esophagogastrectomy and thoracic or TAAA repair [95, 96]. Apart from the extent and duration of surgery, these latter procedures are associated with extended periods of one-lung ventilation, and the operative-side lung is often contused or partially atelectatic despite having been re-inflated at the end of surgery. This leads to hypoxemia and increased work of breathing.

Intraoperative Indications for Postoperative Mechanical Ventilation

Unanticipated operative complications may lead to circumstances that are unfavorable to immediate postoperative extubation. Foremost among these indications are any complications or conditions that lead to difficulty in obtaining adequate oxygenation or CO₂ elimination intraoperatively. Other factors that need to be considered in relation to the list in Table 42.1 are: underlying comorbid conditions, age, and time of day (availability of experts in ventilator and airway management). A period of elective postoperative mechanical ventilation permits stabilization of organ systems (e.g., volume status, cardiac function, coagulation/hemostasis control) while oxygenation and ventilation are assured. Withdrawal of mechanical ventilation can be done in a staged and controlled manner without the pressure of time that exists in the operating room. The list of relative indications in Table 42.6 must be tempered with clinical judgment throughout and at the end of the procedure; continued discussion of the plan with the surgical team can facilitate a smooth transition from the operating room to the PACU or ICU.

Immediate Postoperative Indications for Mechanical Ventilation

As in any surgical patient, circumstances may arise or become evident at the end of thoracic surgery that prevent extubation. Foremost among these are inadequate neuromuscular function as assessed objectively by nerve stimulation or clinically by weakness, and inadequate spontaneous respirations (low rate in association with high end-tidal or arterial CO₂ concentration).

While these complications must be resolved before extubation, of greater concern are problems with oxygenation (e.g., requirement of $\geq 50\%$ FiO_2 to achieve a $\text{SpO}_2 \geq 90\%$), ventilation (inadequate CO_2 elimination despite tachypnea), and visible respiratory distress. Inadequate pain control may contribute to these findings; however, they may also represent a physiologic derangement likely to require more than a few minutes for resolution. Specific blood gas criteria or respiratory measures are frequently quoted as indicating a need for mechanical ventilation; however, in the rapidly changing situation at the end of surgery it is difficult to apply such criteria. A *clinical judgment* must be made to assist or control ventilation for an additional period, usually requiring the patient also be (re)sedated. At this time a call to the PACU or ICU should be made with a request for a mechanical ventilator and sedative infusion(s). A chest radiograph and ABG analysis should be performed at the earliest opportunity.

In addition to permitting the administration of high, known concentrations of oxygen, positive pressure ventilation with PEEP via a tracheal tube assists oxygenation by opening/expanding partially collapsed alveoli and perhaps opening some fully collapsed ones. PEEP improves oxygenation in pulmonary edema and acute lung injury (ALI) both by these mechanisms and by redistributing (but not reducing) lung water [97, 98]. Increasing the fraction of inspired oxygen (FiO_2) will improve arterial oxygenation by increasing transport in those areas that are absorbing O_2 . True shunt will respond only to re-expansion of collapsed segments or reduction of the size of the shunt. This may require bronchoscopy and can be aided by PEEP. Thus, failure of oxygenation is treated with increasing the FiO_2 and/or increasing the mean airway pressure.

Usually the work by the respiratory muscles to ventilate the lungs requires only a few percent of total body oxygen consumption, but this may be several times higher in the postoperative patient, and higher still in acute respiratory failure [99]. Mechanical ventilation also takes over the work of breathing for the patient in distress and guarantees alveolar ventilation. Thus, mechanical ventilation with PEEP treats both components of acute respiratory failure.

Ventilatory Modes

Modern mechanical ventilators used in critical care and now present on anesthesia machines are very sophisticated microprocessor controlled devices that sense and interact with the patient (see Chap. 21). This is in stark contrast to the traditional anesthesia ventilator that has three controls: respiratory rate, tidal volume, and inspiratory flow rate delivering only *volume-cycled*, controlled mandatory ventilation (CMV). Modern ICU ventilators offer a variety of interactive modes, as well as pressure or volume cycled breaths. In addition, many devices administer noninvasive ventilation (NIV), using a specially designed facial or nasal mask (Fig. 42.5) to deliver either CPAP or “BIPAP” which is analogous to pressure support ventilation with PEEP.



FIG. 42.5. Full facemask used to provide CPAP or BIPAP (Respironics/Philips). An air-filled sealing rim provides an occlusive seal around the mouth and nose, with head straps to keep the mask in place as well as provide adequate pressure for the level of CPAP/BIPAP applied. Nasal masks are also available.

Noninvasive Ventilation

As indicated previously, NIV is either CPAP, or Pressure-Support with PEEP (BIPAP) provided via a facemask rather than a tracheal tube. We ventilate our lungs by drawing gas in with our respiratory muscles: during inspiration airway pressure (P_{aw}) is negative with respect to the atmosphere, and during expiration P_{aw} is positive. Spontaneous breathing in this way, but at a positive. Spontaneous rather than atmospheric baseline pressure, is CPAP (Fig. 42.6). Strictly speaking, this is not a mode of ventilation as there is no inspiratory assist. This mode of support is usually used to improve oxygenation in patients who do not have ventilatory failure, as it helps increase the FRC and reduces atelectasis. It may allow spontaneous breathing to occur at a more compliant part of the pressure:volume relationship of the thorax, reducing the work of breathing [100] (Fig. 42.7). CPAP can be provided by a continuous high flow circuit or can be delivered through a microprocessor-controlled ventilator that senses effort (airway pressure or flow) and responds accordingly. In the former case, the airway pressure varies slightly during the respiratory cycle; however, the high level of flow and built in reservoir prevent large swings in pressure. In the latter case, the flow is delivered in response to the sensor, attempting always to meet the patient's demands and to achieve the preset level of CPAP.

An enhancement of CPAP is BIPAP, which provides inspiratory assistance. This mode of NIV can be used in the treatment of acute respiratory failure as well the treatment of hypoxemia. It has been shown to prevent intubation in several medical and surgical populations including thoracic surgery [101]. Several postoperative studies of CPAP and BIPAP have demonstrated benefit and no harm. Squadrone et al. performed a large multicenter trial on patients who had undergone upper abdominal surgery. Patients with a $\text{PaO}_2/$

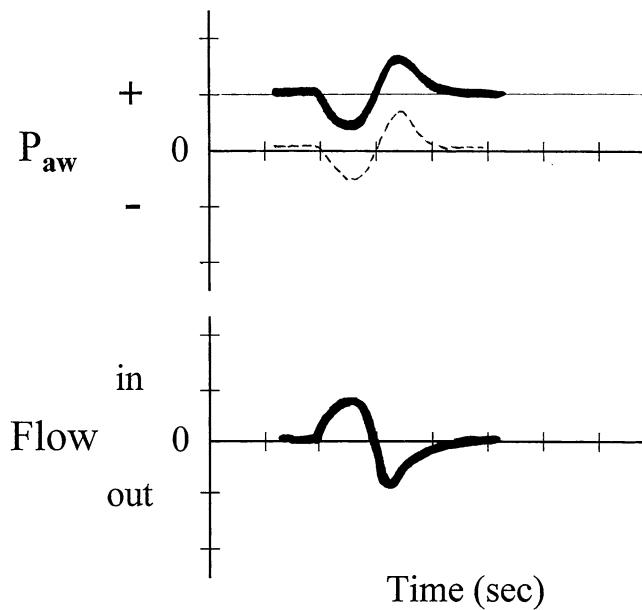


FIG. 42.6. Airway pressure and gas flow during a spontaneous breath through a CPAP mask/circuit: The pressures and flows mirror those for a spontaneous breath (dashed line), but the baseline pressure is elevated. P_{aw} , airway pressure.

FiO_2 ration <300 mmHg were randomized to receive CPAP with an FiO_2 of 0.5 vs. a facemask with FiO_2 of 0.5. Patients receiving CPAP had a lower incidence of reintubation and pneumonia [102]. Another study by Kindgen-Milles looked at postextubation CPAP in patients who underwent open thoracoabdominal aneurysm repair. The patients who received CPAP postextubation had better oxygenation, fewer pulmonary complications, and shorter hospital stay compared to the controls [103]. In a report of 690 patients undergoing lung resection, Lefebvre et al. reported a 16% incidence of respiratory failure, 85% of whom were successfully managed with NIV alone [104]. Perrin et al. used NIV pre and postoperatively and demonstrated a reduction in pulmonary complications after lung resection, Rocco et al. prevented reintubation in 18/21 patients with respiratory failure after lung transplantation, and Michelet et al. showed similar benefits in patients who developed respiratory failure after esophagectomy [105–107].

It is clear that use of CPAP and BIPAP can both prevent and treat respiratory failure after surgery, can avoid the need for intubation, reduce respiratory complications, and decrease length of stay. Surgical concerns for both esophageal and airway anastomoses can be allayed by evidence showing both safety and efficacy, however there are limitations to NIV. It is not appropriate for patients who cannot cooperate or for those with excessive secretions, hemoptysis, or vomiting. Table 42.7 lists contraindications [101]. Success requires patience and expertise on the part of the respiratory therapist, and usually slows incremental increases in both inspiratory and expiratory pressures. The presence of a nasogastric tube may introduce

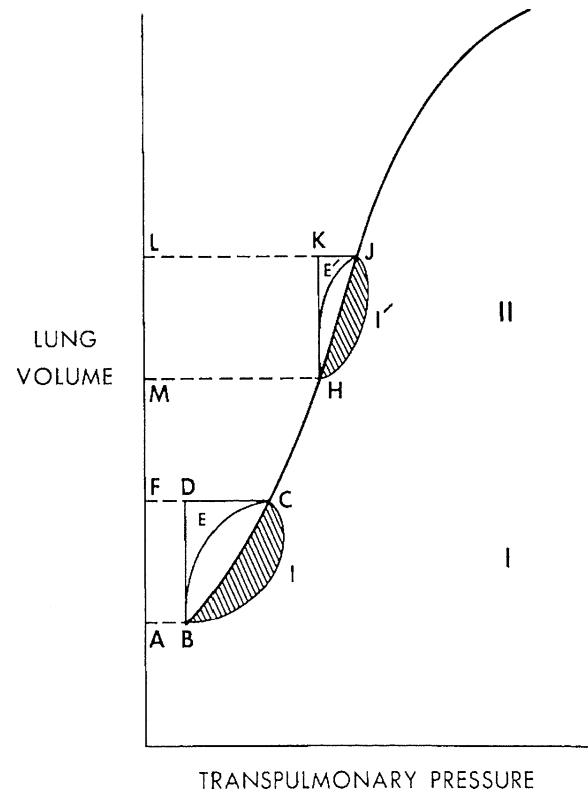


FIG. 42.7. Pressure-volume loops illustrated at two different lung volumes, representing tidal volume at reduced lung volume and FRC as might occur with postoperative atelectasis (A) and the same tidal volume at normal lung volume and FRC (B). The solid sigmoidal line is the elastic pressure-volume curve for the lung and chest wall. Application of CPAP can re-open atelectatic portions of the lung, move tidal breathing up the pressure volume relationship of the lung and chest wall from A to B, both improving gas exchange and reducing the work of breathing (transpulmonary pressure required to generate same tidal volume) (reprinted with permission from Katz and Marks [100]).

TABLE 42.7. Noninvasive ventilation (NIV) after thoracic surgery.

Possible indications

- Prevention of pulmonary dysfunction after lung resection
- Treatment of respiratory failure (short term) after lung resection and lung transplant

Contraindications

CNS

- Decreased level of consciousness
- Severe agitation or encephalopathy
- Uncooperative patient
- Inability to protect airway

Cardiorespiratory

- Cardiac or respiratory arrest
- Cardiac instability
- Severe respiratory failure
- Copious secretions or hemoptysis

Gastrointestinal

- Vomiting/gastric distension
- Upper GI bleeding

Other

- Facial trauma or other condition preventing facemask application
- Multiple organ failure

a leak which cannot be managed, and peak airway pressures (i.e., actual pressure during inspiration) should never exceed 25 cm H₂O. CPAP or BIPAP are not long-term ventilatory modes; if the patient is not clearly improving over a period of 1–2 days then a move to tracheal intubation or tracheotomy should be considered.

Lung Protective Ventilation

The principles of “lung protective ventilation” discussed in Chap. 21 should be adhered to when a decision is made to continue or initiate mechanical ventilation in the postoperative period. If the patient is an appropriate candidate, NIV as described earlier should be seriously considered when a patient who has already been extubated requires oxygenation and/or ventilation assistance beyond what can be offered through facemask oxygen. If mechanical ventilation must be provided through a tracheal tube, appropriate levels of inspiratory pressure and PEEP should be selected. While many strong opinions exist regarding specific modes of ventilation, the ARDSnet trial (referred to below) demonstrated an outcome benefit in ARDS simply employing tidal volumes of 5–8 mL/kg of predicted body weight using assist-control (volume cycled) ventilation and appropriate levels of PEEP. Either pressure or volume modes can be employed so long as delivered tidal volumes are in this range, and airway pressures are not excessive. Pressure modes have the advantage of achieving a similar tidal volume with lower peak airway pressure; however, this has not been shown to translate into an outcome benefit. Table 42.8 summarizes the principles of lung-protective ventilation.

The many possible causes of postoperative respiratory failure have been discussed earlier. In some circumstances, these inciting and predisposing factors can be resolved or compensated for by the patient in the first hours or day after surgery, as the acute stress of surgery subsides and effective analgesic techniques are in place. Mechanical ventilation can then

be withdrawn rapidly and uneventfully. In other patients the interaction of preexisting functional and pulmonary status, surgical stress, and postoperative complications described previously may lead to a more prolonged need for ventilatory assistance. In a small percentage of patients, ALI or ARDS may occur.

Acute Lung Injury and Acute Respiratory Distress Syndrome

As defined by the American-European consensus conference on ARDS, ALI is “a syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension.” ARDS is reserved for the “most severe end of this spectrum” as indicated in Table 42.9 [108].

ALI or ARDS can be induced by direct insults to the lung such as aspiration of gastric contents, pulmonary infection, or contusion, but is more commonly associated with indirect causes such as sepsis syndrome and severe trauma, pancreatitis, or massive transfusion. The latter causes are typically referred to as “extrapulmonary.” Mortality implications are similar with direct pulmonary injury or extrapulmonary causes [109, 110]. It is uncommon to see the diffuse infiltrates that characterize ALI and ARDS immediately after surgery; such a finding on the postoperative radiograph is more likely to represent hydrostatic edema due to fluid overload or left-sided cardiac failure. Hydrostatic pulmonary edema may be radiographically indistinguishable from ALI and ARDS, at least in the early stages.

Direct injury to the lung as a result of surgery or indirect effects from other organ system dysfunctions, trauma of surgery, or multiple transfusions may initiate the pathophysiology leading to ALI and ARDS in thoracic surgery patients. In a 6-year review (1991–1997) of all pulmonary resections done at the Royal Brompton Hospital in London, England, the combined incidence of ALI and ARDS was 3.9%. The overall mortality from ARDS is approximately 50%, although recent data suggests a decline over the last 10 years; in the review from the Royal Brompton Hospital ALI/ARDS was associated with 72.5% of the mortality [111]. Patients with the syndrome typically go on to have other organ dysfunctions, developing the multiple organ dysfunction syndrome

TABLE 42.8. Principles of “lung protective” ventilation.

Ventilator mode	Volume assist-control most often reported
Tidal volume (mL/kg of predicted body weight)	5–7 (lower is better)
Plateau pressure (cm of water)	≤30
Ratio of duration of inspiration to expiration	1:1–1:3
Ventilator rate (breaths/min)	Set to achieve pH>7.3
Bicarbonate infusion	As needed if pH goal cannot be achieved
Oxygenation goal	PaO ₂ >55 mmHg or SpO ₂ >88%
PEEP	As needed to achieve oxygenation goal (titrated upwards with FiO ₂) ^a

^a See ref. [122] for protocol describing incremental adjustments of FiO₂ and PEEP

TABLE 42.9. Definition of ARDS and ALI.

Acute onset clinical syndrome of hypoxemia as follows	
ARDS	PaO ₂ /FiO ₂ ≤300 mmHg regardless of PEEP Bilateral patchy infiltrates on chest radiograph No evidence nor suspicion of left heart failure
ALI	PaO ₂ /FiO ₂ ≤200 mmHg regardless of PEEP Bilateral patchy infiltrates on chest radiograph No evidence nor suspicion of left heart failure

or “MODS” [112]. In fact, most patients who succumb do so of nonrespiratory organ failures [113]. The MODS syndrome occurs in approximately 15% of ICU patients and is responsible for 80% of ICU deaths [114]. Rather than the severity of gas exchange abnormality in ARDS, other patient-specific factors such as preexisting organ system dysfunction, increasing age, and the presence of sepsis that are more predictive of mortality. As more systems become involved in the MODS, mortality increases exponentially. Patients who survive ARDS are likely to have relatively intact pulmonary function within 6–12 months, although health-related quality of life is reduced [115]. If the lung injury in ARDS does not resolve in 7–10 days, it may progress to fibrosis, and finally to obliteration of the pulmonary capillary bed with pulmonary hypertension.

Therapy of ALI and ARDS

Despite more than 30 years of research into causes and treatment of ALI and ARDS, it remains a clinical syndrome with elusive etiology. A great deal of progress has been made in understanding the pathophysiology; however, the earliest events which trigger the inflammation and damage of lung tissue continue to be explored. Therapy targeting these early events, and pharmacotherapy in general, has been disappointing. A variety of pharmacological agents including prostaglandins, surfactant, inhaled nitric oxide (NO), and corticosteroids have failed to demonstrate an outcome benefit [116–119]. Current treatment of ARDS is therefore “supportive,” attempting to provide vital organ support without further damaging the lungs and providing an environment for healing. As a pulmonary dilator, inhaled NO can reduce pulmonary artery pressure without causing systemic hypotension, and improves oxygenation by augmenting blood flow to ventilated alveoli, but these benefits have failed to improve survival.

Mechanical Ventilation with PEEP

Perhaps one of the most surprising outcomes of the intense research into ARDS has been the gradual realization that the mainstay of therapy itself – mechanical ventilation – could worsen, and even in some animal models actually *cause*, lung injury. More than 25 years ago, ventilation with high volumes and pressures was shown to cause pulmonary edema in animal models [120]. Further studies documented such injury in a variety of animal models and settings, and in particular the worsening of existing injury with high volumes. Inflammatory markers are elevated when high volumes are used to ventilate patients with ARDS, and survival from the syndrome can be improved by using small (6–8 vs. 10–12 mL/kg) tidal volumes [121]. The “ARDSnet” trial funded by the National Heart, Lung and Blood Institute in the United States, and performed by the “ARDS network” of institutions, documented a mortality reduction from almost 40 to 31% by simply using a smaller tidal volume to achieve a “plateau pressure” of ≤ 30 cm H₂O, in association with a protocolized strategy for FiO₂, PEEP, and

management of acid–base disorders [122]. This approach to ventilation has been termed “lung protective.” An overview of the protocol is given in Table 42.8 and can be found at <http://www.ardsnet.org> [122]. Evidence from this trial, other clinical and laboratory studies, and now a number of perioperative studies as described in Chap. 21 have resulted in a general move to the use of smaller tidal volumes in all ventilated patients, both in the OR and the ICU.

Collapse and re-expansion of alveoli with each respiratory cycle can cause injury, and this can be reduced or prevented by adequate levels of PEEP [123]. Determining the optimal level of PEEP has concerned clinicians for more than 25 years and continues to be a dilemma. In 1975, Suter et al. coined the phrase “best PEEP” in relating the PEEP level to oxygen delivery to the tissues (Fig. 42.8) [124]. These investigators found that although increasing levels of PEEP usually resulted in better oxygenation of the arterial blood, as the intrathoracic pressure rose above a certain level the cardiac output and hence oxygen delivery declined. In recent years, while taking

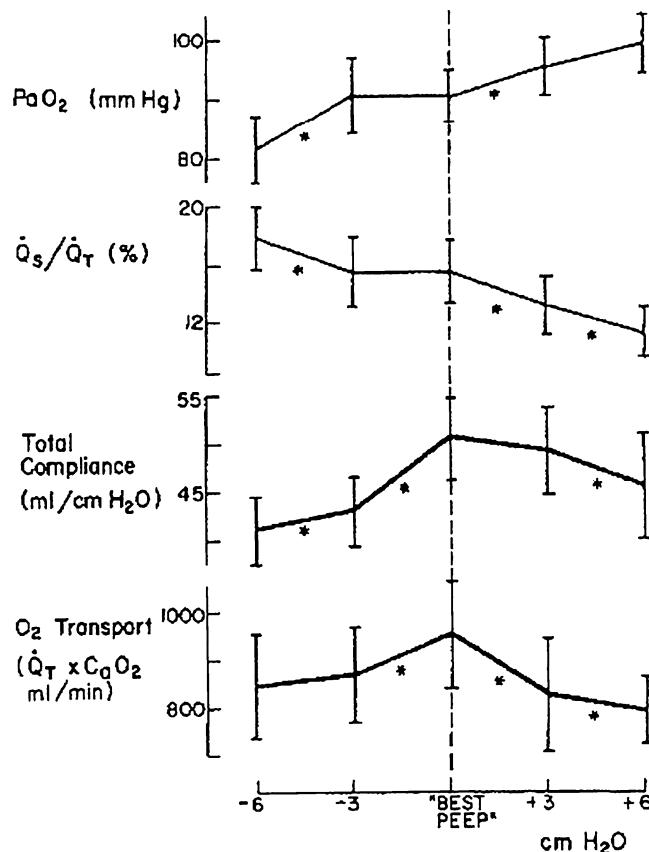


FIG. 42.8. Illustration of how the level of PEEP associated with the best oxygen (O₂) transport (“best PEEP”) may not be the level associated with the highest arterial pO₂ or lowest shunt fraction (Q_s/Q_t). As the PEEP is increased above the “best” level (different in different patients), O₂ transport decreases as a result of decreased preload and cardiac output (reprinted with permission from Suter et al. [124]).

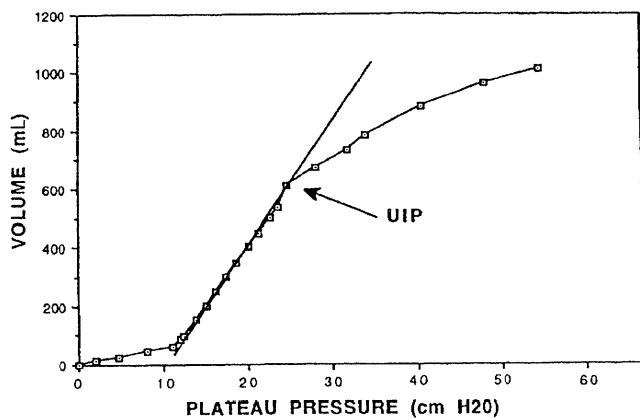


FIG. 42.9. A pressure–volume curve of the respiratory system in a patient with ARDS. Ideally ventilation should occur at a lung volume represented by the middle section of the curve where the lung is most compliant. If ventilation occurs at a lung volume overlapping either the LIP or upper inflection point (UIP), ventilator-induced trauma may occur. In the former case this is due to repeated opening and closing of alveoli due to inadequate level of PEEP; in the latter it is overdistending of already fully inflated alveoli (reprinted with permission from Roupie et al. [125]).

this latter concept into consideration, there has been a greater interest in finding the level of PEEP that keeps the most alveoli open, ventilating only on the compliant portion of the pressure–volume relationship of the lung. The theoretical goal is to use adequate PEEP such that ventilation occurs above the “lower inflection point” (LIP) of the pressure–volume relationship as shown in Fig. 42.9, using a tidal volume that is below the upper inflection point [125]. This requires some measure of the pressure–volume relationship which may not always be possible. In a follow-up study to the ARDSnet trial, a randomized trial of lower vs. higher PEEP was performed. In this study the PEEP was increased more rapidly in the high PEEP group, usually exceeding 12 cm H₂O and there was no influence in outcome [126]. A more recent meta-analysis suggests that higher PEEP (>10 cm H₂O) may provide a small benefit, especially when lung injury is more severe – ARDS vs. ALI [127]. It may be that higher levels are most useful in patients where there is a clear beneficial effect in terms of improved oxygenation and compliance.

As the practice of using reduced tidal volumes has increased, two clinical problems have become apparent. The first is the need for high respiratory rates to achieve normal arterial CO₂ levels, and sometimes failing to achieve the latter. The phrase “permissive hypercapnia” has been coined, meaning that a higher than normal CO₂ level is tolerated in order to protect the lung from high tidal volume ventilation [128]. Either the respiratory acidosis is tolerated or a bicarbonate infusion can be used to restore the pH towards normal. In the ARDSnet trial, a pH of 7.30 was tolerated; in other studies even lower

levels have been accepted. The second problem is that despite relatively high PEEP levels, the use of small tidal volumes may result in gradual collapse of alveoli and worsened oxygenation. This has led to the investigation of “recruitment” maneuvers such as intermittent application of high levels of airway pressure, analogous to the old concept of sighs. Recent work suggests that such recruitment maneuvers can improve oxygenation in ARDS but there are no studies which address an outcome benefit [129].

Positive intrathoracic pressure may have an impact on cardiac performance. With relatively compliant lungs, positive pressure created by the ventilator is transmitted to the entire thoracic cavity and may affect the preload and afterload to the heart. If cardiac function is normal, the predominant effect is a reduction in venous return leading to a decrease in cardiac output. As indicated earlier, this is illustrated in Fig. 42.8 where the “best PEEP” was the level at which the increase in oxygenation of the blood was not offset by a reduction in cardiac output [124]. Where there is left ventricular dysfunction and elevated filling pressure, the reduction in preload may reduce ventricular distension and improve cardiac performance. In addition, making the intrathoracic cavity positive with respect to the rest of the body reduces the afterload to the left ventricle (Fig. 42.10) [130].

Right ventricular function may be adversely affected by high levels of PEEP (e.g., >10 cm H₂O). The right ventricle is a thin-walled cavity that normally generates relatively low pressures (e.g., 25 mm Hg systolic). High levels of PEEP required to oxygenate the blood may increase the impedance to right ventricular ejection, causing right ventricular dilatation and a decrease in contractility [131]. In patients who have undergone pulmonary resection, in particular pneumonectomy, the right ventricle is already “stressed” by needing to pump the normal cardiac output through a reduced pulmonary vascular tree. Overdistension of the right ventricle may distort the interventricular septum, interfering with left ventricular filling [132]. Echocardiographic assessment of ventricular function, pulmonary artery catheterization, or cardiac output measurement by “stand alone” devices may be useful to determine the effect of mechanical ventilation on cardiac performance.

Another undesirable feature of positive pressure ventilation is the creation or worsening of “autoPEEP,” where partially obstructed airways prevent complete emptying of the alveoli during expiration. This results in continued gas flow and airway pressure above baseline (i.e., atmospheric or whatever level of PEEP is applied) at the end of expiration. Application of additional PEEP can “match” the autoPEEP and reduce the patient effort required to initiate a spontaneous breath or trigger a machine breath. If, however, a rapid respiratory rate is set on the ventilator and/or lung pathology causes reduced expiratory flow rates not permitting the lung to fully empty with expiration, autoPEEP is worsened with positive pressure ventilation.

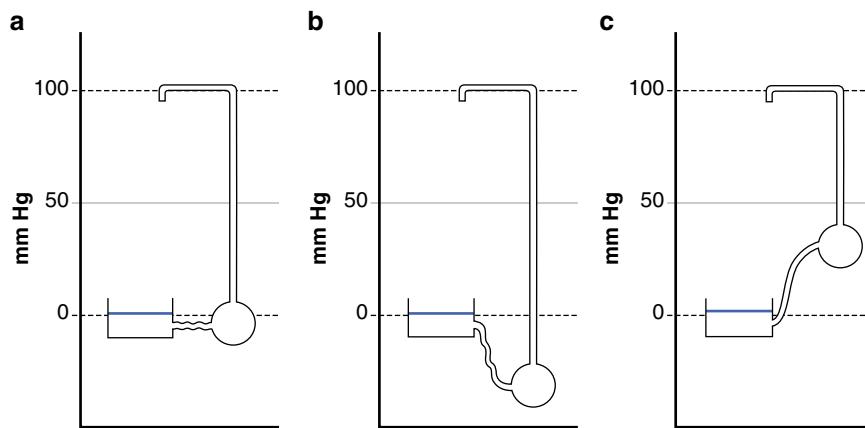


FIG. 42.10. Diagrammatic representation of the effects of respiratory induced changes in pleural pressure on right ventricular inflow and left ventricular outflow. At end-expiration (a) the venous reservoir empties at normal pressure into the heart which generates normal systemic pressure. With deep inspiration (b) venous inflow is augmented because the intrathoracic pressure (location of the heart) is made negative; at the same time the heart must generate a higher pressure to achieve a normal systemic pressure outside of the thorax. During expiration (c) venous inflow is reduced at the same time as left ventricular afterload is reduced. This illustrates the mechanism of the beneficial effects of positive intrathoracic pressure (positive pressure ventilation, PEEP) in patients with heart failure.

Prone Position

In 1974, Bryan proposed that during mechanical ventilation the dorsal regions of the lung would receive improved ventilation in the prone position [133]. Since that time a variety of publications have demonstrated his theory correct. Both animal and human studies have demonstrated improved matching of ventilation to perfusion, as well as overall better distribution of blood flow and transpleural pressures gradients [134, 135]. An elegant study demonstrated the dramatic effects of prone positioning on regional lung density with serial CT scanning [136]. While the majority of studies of the prone position in the setting of ALI and ARDS have demonstrated an improvement in oxygenation, outcome studies have been inconclusive or disappointing. A recent meta-analysis reached this same conclusion: improved oxygenation but no effect on survival, and there was a reduction in ventilator-associated pneumonia [137]. Use of the prone position in a critically ill patient can be a challenge to the clinical staff.

Alternate Modes of Ventilation

A variety of modes of ventilation including inverse ratio (where inspiration is longer than expiration), airway pressure release ventilation (APRV, spontaneous breathing at high airway pressure, with intermittent release), high frequency oscillatory ventilation (HFOV, very small tidal volume and high frequency), and high frequency percussive ventilation (HFPV, high frequency “stacking” breaths resulting in lower frequency convective breaths) have been described and evaluated in small clinical studies. Inverse ratio ventilation and APRV are modes available on commercial ventilators; HFOV and HFPV require specialized ventilators. All of these modes have been used to improve oxygenation and/or ventilation;

however, there is a paucity of outcome studies [138]. There is some suggestion that early use of HFOV, for example, may provide a benefit in ALI/ARDS; however, these modes are generally “end of the road” strategies when conventional ventilatory modes have failed.

Extracorporeal Membrane Oxygenation (ECMO)

Recent experience with ECMO in adults, as reported by the Extracorporeal Life Support Organization (ELSO), is likely to result in a renewed interest in this mode of therapy for ARDS. In their 2008 report, survival to hospital discharge or transfer in adults where ECMO was initiated for respiratory failure, was an impressive 51% [139]. The majority of these patients had ARDS. Similarly, in a report of 22 patients receiving ECMO for primary graft dysfunction after lung transplantation, the survival was 54% at 1 year [140]. Patients with a potentially reversible cause of respiratory failure and a PaO_2 to FiO_2 ratio of <100 should be referred to an ECMO center, and when this ratio drops below 70 this should be considered an indication to institute the therapy [141]. Other than lung transplantation there is little published experience in postoperative thoracic surgery patients. ECMO is discussed in detail in Chap. 43.

Complications of Mechanical Ventilation

Trauma to the Lungs or Tracheobronchial Tree

Damage to the lung parenchyma as a consequence of mechanical ventilation is discussed earlier. In thoracic surgery patients, the potential risk of suture line or bronchial stump disruption as a result of positive airway pressure has also been referred to. Suture line disruption can cause catastrophic pneumothorax

or respiratory failure, or may result in chronic air leak, bronchopleural fistula, and infection. Avoidance of intubation and positive pressure ventilation are certainly desirable, but not always possible. As discussed earlier, use of pressure-limited modes of ventilation, and use of small tidal volumes if volume-controlled modes are used may help avoid high pressures. Auriant et al. suggested that NIV could reduce the mortality in acute respiratory failure after pneumonectomy [142].

Ventilator-Associated Pneumonia

One of the most serious complications associated with mechanical ventilation is pneumonia. Ventilator-associated pneumonia (VAP) is defined as pneumonia developing >48 h after initiating mechanical ventilation with absence prior to intubation. The reported incidence varies from 8 to 28% of patients receiving mechanical ventilation for more than 48 h, which is approximately 3–10-fold the incidence of pneumonia in nonintubated hospitalized patients [143–146]. Current reporting techniques use the relationship between number of ventilator days and incidence of pneumonia, with surgical units experiencing 9–10 pneumonias per 1,000 ventilator days [147]. The mortality is reported from 24 to 50%, and can be up to 76% in specific settings with high-risk pathogens. Resistant organisms comprise an ever increasing proportion of hospital acquired infections, including VAP [148].

Diagnosis

VAP should be suspected when there is a new or changing infiltrate on chest X-ray, and at least two of: abnormal temperature ($>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$), abnormal white blood cell count ($>10,000$, $<4,000$, or with $>10\%$ immature cells), and purulent sputum. Bronchoalveolar lavage or protected specimen brush by FOB can be used to obtain a culture sample to more positively identify the pathogenic organism. However, a randomized study in 740 patients failed to demonstrate improved outcome if bronchoscopic sampling rather than simple tracheal tube suction was the initial culture technique [149]. Most important is the early initiation of appropriate institution-based empiric broad-spectrum antibiotics, as failure to adequately treat from the earliest possible opportunity is associated with worsened outcome. The presence of resistant organisms in the institution or specific ICU determines which agents should be chosen at the outset.

Prevention

Prevention of VAP is a priority in modern intensive care. This has given rise to the concept of the ventilator or VAP “bundle” – a variety of care processes either known or believed to reduce the risk of acquiring VAP [150]. These measures include elevation of the head of the bed to 30° to reduce aspiration risk, oral rinse with antiseptic solution to reduce bacterial load, daily withdrawal of sedation, and daily spontaneous

breathing trials (SBTs) to facilitate removal of the tracheal tube. Prophylaxis for stress ulceration and deep venous thrombosis are often included in the “bundle.” Continuous aspiration of subglottic secretions (CASS) has been evaluated with the goal of preventing aspiration. CASS requires a specialized ETT with a second lumen allowing a suction catheter proximal to the endotracheal tube cuff. Bouza et al. were able to demonstrate a reduction in VAP in patients treated with CASS [151]. Coating an endotracheal tube with silver has also been investigated and is theoretically attractive because of silver’s broad-spectrum antimicrobial activity. A recent investigation by Kollef et al. with silver coated endotracheal tubes was able to demonstrate a reduction in the incidence of VAP [152].

Withdrawal of Mechanical Ventilation

Many factors play into the decision to withdraw ventilatory support, the first being adequate control or resolution of the condition which lead to the need for ventilation. In the postoperative thoracic surgery patient, this may simply be correction of acute issues such as pain control, fluid status, and temperature. If gas exchange has been the principal issue, then ability of the patient to achieve acceptable pH, pCO_2 and pO_2 , or saturation must be assessed. In general, the need for positive pressure ventilation with more than 50% oxygen and/or 5–8 cm H_2O of PEEP to obtain a pO_2 of 60 mmHg or saturation of >90% suggests that oxygenation will not be adequate without ventilatory support. Similarly, elevated pCO_2 in association with decreased pH suggests either oversedation or inadequate ventilatory capacity. Medical problems that may contribute to respiratory failure (e.g., heart failure) should be stable or controlled, and the patient should be responsive and able to clear secretions. Requirement for frequent (e.g., more than every 2 h) suctioning, fever, or significant inotropic or vasopressor therapy all suggest the patient may not be ready for withdrawal of respiratory support. Once these considerations have been addressed, a “physiological” assessment needs to be performed to see if the patient is able to breathe spontaneously without distress. The most common of these is the “rapid shallow breathing index” where the patient is allowed to breathe without support for a few minutes, and the index is computed by dividing the breathing frequency by the tidal volume. An index of >100 strongly predicts failure of a longer duration SBT; a value of less than this does not necessarily predict success [153].

Analogous to the startling revelation that a relatively modest change in ventilator management (reduced tidal volume with adequate PEEP) leads to improved survival in ARDS, performing a 30–120 min SBT on appropriate patients through a “T-piece” or with low-level CPAP and/or pressure support identifies a large number of patients who are ready to be extubated. Two large trials indicated that clinicians did not recognize that discontinuing support would be possible in more than two thirds of the patients who were successfully identified with a SBT [154, 155]. These studies found that

TABLE 42.10. The spontaneous breathing trial.

Indication	Daily assessment of readiness to separate from mechanical ventilation
Criteria to perform	<ul style="list-style-type: none"> – At least partial resolution of underlying condition(s) leading to respiratory failure – Conventional ventilation mode (volume or pressure) – Absence of respiratory distress – Sedation infusions withdrawn (daily withdrawal) and patient responsive – No CNS contraindications (e.g., elevated intracranial pressure) – $\text{SpO}_2 \geq 88\%$ with $\text{FiO}_2 \leq 0.5$ and $\text{PEEP} \leq 8$ – Minimal cardiovascular support (e.g., inotropes/pressors) not increasing – Rapid shallow breathing index (RSBI) $<100^a$ in first minutes of trial
Criteria for failure	<p>Clinical</p> <ul style="list-style-type: none"> – Change in mental status, usually agitation/anxiety – Visible distress such as diaphoresis, increasing effort <p>Objective</p> <ul style="list-style-type: none"> – Decreasing SpO_2 (below 88%) or increasing end-tidal CO_2 – Increasing tachypnea (>35 breaths/min) – Increasing tachycardia ($>140/\text{min}$) or other dysrhythmia, and/or hypertension – RSBI^a increasing to >100 – Blood gas if drawn with $\text{SaO}_2 < 88\%$; $\text{P}_a\text{CO}_2 > 10$ mm above baseline, and $\text{pH} < 7.32$

^aRespiratory rate (breaths/min) divided by tidal volume (in liters), with no support or 5 cm pressure support/5 cm PEEP

a SBT reduced the duration of mechanical ventilation when compared to other techniques such as gradual withdrawal of IMV or pressure support. The report of a consensus meeting suggested that a 30–120 min SBT is the “major diagnostic test to determine whether patients can be successfully extubated” [156]. Psychological support, encouragement, and physical presence of a caregiver at the bedside for at least the early part of the trial are essential. Criteria for performing an SBT are summarized in Table 42.10.

SBTs also identify patients who are *not* ready for withdrawal of ventilator support; Table 42.10 lists criteria for failure of a SBT. Of those patients who fail an initial trial, most will eventually succeed in the following week. A daily SBT identifies these patients. There will be a small percentage of patients who require prolonged care and possibly require transfer to a “weaning facility” or “long-term acute care” (LTAC) facility. When a patient fails a SBT, the reasons for failure need to be carefully examined. They may include inadequate resolution of the primary or underlying problem, weakness (e.g., nutritional depletion), or inadequate recovery from sedation to name a few. Between SBTs, patients should be supported with a mode of ventilation which requires spontaneous but nonfatiguing efforts by the patient as atrophy and weakness of respiratory muscles develops within less than 24 h of complete

ventilatory rest [157]. Malnutrition is increasingly recognized as a contributor to weakness in ventilated patients, and some form of nutrition needs to be addressed in the patient who requires mechanical ventilation for more than a few days.

Daily interruptions of sedative infusions decrease the duration of mechanical ventilation [158]. This is best accomplished by use of a sedation protocol, which has also been shown to reduce the duration of mechanical ventilation [159–161]. A significant issue in the ventilated patient is delirium, which is multifactorial (e.g., pain, sleep deprivation, polypharmacy) and may be associated more with benzodiazepines than other sedative drugs. When it occurs, delirium is associated with significantly worsened outcome [162].

Extubation

Separate from weaning and the requirement for ventilatory assistance, readiness for extubation requires its own assessment. The patient must be awake and cooperative, able to cough and clear secretions, and the airway must be patent. In a study by Khamiees et al., poor cough strength and increased amounts of respiratory secretions were synergistic in predicting extubation failure [163]. While there is no perfect way of assessing airway patency, a “cuff leak” test can be performed in a subjective or objective manner. For the former, the clinician simply deflates the cuff on the tube and listens for audible air leak during either spontaneous breathing or with positive pressure ventilation. Absence of an audible leak suggests airway edema and the potential for postextubation obstruction. This is more likely with prolonged intubation, trauma, obesity, or female gender [164]. The test can be quantified by measuring the volume lost during volume-controlled ventilation although another group of investigators did not find the test useful in surgical patients [165, 166]. If a cuff test of any kind suggests minimal or absent air leak, but a decision is made to proceed with extubation, a “tube changer” should be used to allow urgent reintubation.

Tracheostomy

When the period of mechanical ventilation is likely to be more than 7–10 days, there are several reasons why tracheotomy is a favored approach. First and possibly most important, it allows for a greater degree of comfort by removing the transoral or transnasal tube and associated holding device or tape. This alone can result in a reduced need for sedation. By introducing a permanent path into the airway, the need for physical restraint is reduced and the patient can be mobilized (e.g., to a chair) with less risk and greater ease. The patient may be able to swallow liquid or solid food at an earlier stage, and may be able to speak during periods when there are off the ventilator (with the use of a one-way “Passey-Muir” valve). Replacement of the relatively long transoral or transnasal tube with a much shorter tracheotomy tube reduces the imposed airways resistance and facilitates removal of secretions [167].

In patients projected to need ventilation >2 weeks, Rumbak et al. demonstrated early tracheostomy resulted in lower mortality, fewer cases of VAP, fewer accidental extubations, and less time spent on mechanical ventilation than a late tracheostomy strategy [168]. A recent study failed to demonstrate a benefit in terms of VAP with early tracheotomy performed at 6–8 days vs. later tracheotomy at 13–15 days, but other trials have failed to demonstrate a benefit in terms of speed of weaning [169]. In the thoracic surgery patient, the surgeon may prefer to perform his/her own surgical tracheotomy in the operating room; however, there are now many studies attesting to the safety and cost savings of bedside percutaneous tracheotomy [170, 171]. In many of these studies, intensivists performed the tracheotomy in medical ICUs.

Clinical Case Discussion

A 65-year-old male is in the PACU after undergoing open right upper lobectomy for squamous cell carcinoma. He has a long history of smoking, and his preoperative room air saturation was 91%. He is tachypneic, slightly lethargic, and complaining of pain; his peripheral saturation reading is 88% and he is receiving 100% oxygen by facemask. His blood pressure is 160/100 and heart rate 105/min.

Questions

- What are the likely diagnoses?
- Which (if any) diagnostic tests should be obtained?
- Which treatment modalities should be employed, and in what order?

Answers

- Residual neuromuscular blockade, pain with splinting and resultant low tidal volume, and mechanical complications such as pneumothorax or lobar atelectasis are all possibilities, alone or in combination. Pulmonary edema as a result of cardiac disease and/or volume overload is also possible.
- Assessment of neuromuscular function clinically or with “train-of-four” should be made. The lungs should be auscultated and a portable chest radiograph should be obtained to determine if edema or a mechanical problem is present. An ABG should be obtained to determine pCO_2 and pH.
- Application of CPAP or BIPAP may acutely relieve respiratory distress and improve oxygenation if the patient is cooperative. An inhaled bronchodilator may be indicated if the patient is known to have a response and/or if rhonchi or wheezing are audible. Treatment of pain may be important, but may also reduce respiratory drive. Appropriate intervention should be made for a mechanical problem.

The chest radiograph demonstrates partial collapse of the right lower lobe, and the patient becomes agitated with the

application of BIPAP. The blood pressure is now 180/110, and the saturation remains between 85 and 90%. The ABG shows a pO_2 of 55 mmHg, pCO_2 of 60 mmHg, and pH of 7.25.

Question

- What should be done now?

Answer

- The blood gas confirms a diagnosis of respiratory failure of both oxygenation and ventilation. Lobar atelectasis may be resolved with vigorous coughing and “physiotherapy” maneuvers such as percussion, postural drainage, and positive pressure breathing; however, in this acute setting of an agitated patient unable to tolerate positive pressure, most likely intubation is required. In addition, early postoperative lobar atelectasis may be due to retained secretions and is an indication for FOB. In this patient, bronchoscopy will require intubation.

The patient is intubated uneventfully and bronchoscopy is performed where significant tenacious secretions are aspirated from the right bronchus intermedius. The arterial saturation rises to 95% on 100% FiO_2 .

Questions

- What ventilator settings should be used?
- Should the patient be prepared for extubation?
- Should broad spectrum antibiotics be employed?

Answers

- This patient is at risk for ventilator-induced lung injury due to underlying disease, pulmonary surgery, and now a postoperative pulmonary complication (see Chap. 21). He should be managed with a lung-protective strategy which includes appropriate PEEP (usually 5–10 cm H_2O) and a tidal volume of 5–7 mL/kg of predicted body weight. The goal is a “plateau” pressure of 30 cm H_2O or less. Ideally a ventilator mode which allows/assists spontaneous efforts should be used. As lobar atelectasis was present before the bronchoscopy, a “recruitment maneuver” should be considered.
- Assessment for ventilator wean and extubation is a clinical judgment based on a variety of factors. If the patient is easy to ventilate and oxygenate, and appears otherwise well recovered from the complication, then sedation may be withdrawn, a physiologic assessment for rapid shallow breathing made, and a SBT performed. As the patient has a peripheral saturation of only 95% on 100% oxygen, it is more likely he will need a period of positive pressure ventilation with PEEP before meeting oxygenation requirements for an SBT.
- If the patient was not hospitalized before surgery then the likely pathogens in his sputum are “community acquired.”

The local experience will dictate which antibiotic should be considered, in addition to or instead of the usual surgical prophylaxis. If the patient is an inpatient or was recently hospitalized, then antibiotics appropriate for the hospital experience (such as vancomycin for methicillin resistant *S. aureus*) should be considered. Pneumonia, and especially ventilator-associated pneumonia (VAP) is associated with a high mortality but there are no data regarding the administration of “prophylactic” antibiotics in a situation such as this. It may be more prudent to obtain a lower airway sample for culture, stay with the usual perioperative prophylaxis, and initiate appropriate antibiotics if a pulmonary infection appears to be developing.

References

1. Hirschler-Schulte CJ, Hylkema BS, Meyer RW. Mechanical ventilation for acute postoperative respiratory failure after surgery for bronchial carcinoma. *Thorax*. 1985;40(5):387–90.
2. Busch E et al. Pulmonary complications in patients undergoing thoracotomy for lung carcinoma. *Chest*. 1994;105(3):760–6.
3. Stephan F et al. Pulmonary complications following lung resection: a comprehensive analysis of incidence and possible risk factors. *Chest*. 2000;118(5):1263–70.
4. Wada H et al. Thirty-day operative mortality for thoracotomy in lung cancer. *J Thorac Cardiovasc Surg*. 1998;115(1):70–3.
5. Harpole Jr DH et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg*. 1999;117(5):969–79.
6. Harpole DH et al. Prospective analysis of pneumonectomy: risk factors for major morbidity and cardiac dysrhythmias. *Ann Thorac Surg*. 1996;61(3):977–82.
7. Kane RD, Rasanene J. Hypoxemia. In: Kirby RR, Gravenstein N, editors. *Clinical anesthesia practice*. Philadelphia: WB Saunders Company. 1994;782.
8. West JB. Pulmonary pathophysiology, the essentials. 3rd ed. Baltimore: Williams and Wilkins; 1977.
9. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc*. 1984;59(1):17–20.
10. Dewan NA et al. Persistent hypoxemia due to patent foramen ovale in a patient with adult respiratory distress syndrome. *Chest*. 1986;89(4):611–3.
11. Vaughn GC, Downs JB. Perioperative pulmonary function, assessment, and intervention. *Anesthesiol Rev*. 1990;17:19–24.
12. Arozullah AM et al. Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. *Ann Surg*. 2000;232(2):242–53.
13. Dales RE et al. Preoperative prediction of pulmonary complications following thoracic surgery. *Chest*. 1993;104(1):155–9.
14. Cywinski JB et al. Predictors of prolonged postoperative endotracheal intubation in patients undergoing thoracotomy for lung resection. *J Cardiothorac Vasc Anesth*. 2009;23(6):766–9.
15. Smetana GW. Preoperative pulmonary evaluation. *N Engl J Med*. 1999;340(12):937–44.
16. Epstein SK et al. Predicting complications after pulmonary resection. Preoperative exercise testing vs a multifactorial cardiopulmonary risk index. *Chest*. 1993;104(3):694–700.
17. Global Initiative for Asthma, 2009 Revision. www.ginasthma.org/application.asp. Accessed 15 July 2010.
18. Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. Perioperative total parenteral nutrition in surgical patients. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. *N Engl J Med*. 1991;325(8):525–32.
19. Landreneau RJ et al. Acute and chronic morbidity differences between muscle-sparing and standard lateral thoracotomies. *J Thorac Cardiovasc Surg*. 1996;112(5):1346–50. discussion 1350–1.
20. Ginsberg RJ et al. Modern thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg*. 1983;86(5):654–8.
21. Imperatori A et al. Peri-operative complications of video-assisted thoracoscopic surgery (VATS). *Int J Surg*. 2008;6 Suppl 1:S78–81.
22. Flores RM, Alam N. Video-assisted thoracic surgery lobectomy (VATS), open thoracotomy, and the robot for lung cancer. *Ann Thorac Surg*. 2008;85(2):S710–5.
23. Villamizar NR et al. Thoracoscopic lobectomy is associated with lower morbidity compared with thoracotomy. *J Thorac Cardiovasc Surg*. 2009;138(2):419–25.
24. Cooper JD et al. Results of 150 consecutive bilateral lung volume reduction procedures in patients with severe emphysema. *J Thorac Cardiovasc Surg*. 1996;112(5):1319–29. discussion 1329–30.
25. Naunheim KS et al. Predictors of operative mortality and cardiopulmonary morbidity in the National Emphysema Treatment Trial. *J Thorac Cardiovasc Surg*. 2006;131(1):43–53.
26. Fujimoto T et al. Long-term results of lung volume reduction surgery. *Eur J Cardiothorac Surg*. 2002;21(3):483–8.
27. National Emphysema Treatment Trial Research Group. Patients at high risk of death after lung-volume-reduction surgery. *N Engl J Med*. 2001;345(15):1075–83.
28. Drachman DB. Myasthenia gravis (first of two parts). *N Engl J Med*. 1978;298(3):136–42.
29. Eisenkraft JB et al. Predicting the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology*. 1986;65(1):79–82.
30. Moore KH et al. Thymoma: trends over time. *Ann Thorac Surg*. 2001;72(1):203–7.
31. Karl RC et al. Factors affecting morbidity, mortality, and survival in patients undergoing Ivor Lewis esophagogastrectomy. *Ann Surg*. 2000;231(5):635–43.
32. Ellis Jr FH et al. Esophagogastrectomy for carcinoma of the esophagus and cardia: a comparison of findings and results after standard resection in three consecutive eight-year intervals with improved staging criteria. *J Thorac Cardiovasc Surg*. 1997;113(5):836–46. discussion 846–8.
33. Alexiou C et al. Surgery for esophageal cancer in elderly patients: the view from Nottingham. *J Thorac Cardiovasc Surg*. 1998;116(4):545–53.
34. Bailey SH et al. Outcomes after esophagectomy: a ten-year prospective cohort. *Ann Thorac Surg*. 2003;75(1):217–22. discussion 222.
35. Atkins BZ et al. Reducing hospital morbidity and mortality following esophagectomy. *Ann Thorac Surg*. 2004;78(4):1170–6. discussion 1170–6.
36. Money SR et al. Risk of respiratory failure after repair of thoracoabdominal aortic aneurysms. *Am J Surg*. 1994;168(2):152–5.
37. Svensson LG et al. A prospective study of respiratory failure after high-risk surgery on the thoracoabdominal aorta. *J Vasc Surg*. 1991;14(3):271–82.

38. Etz CD et al. Pulmonary complications after descending thoracic and thoracoabdominal aortic aneurysm repair: predictors, prevention, and treatment. *Ann Thorac Surg.* 2007;83(2):S870-6. discussion S890-2.
39. Woo SW, Berlin D, Hedley-Whyte J. Surfactant function and anesthetic agents. *J Appl Physiol.* 1969;26(5):571-7.
40. Duggan M, Kavanagh BP. Pulmonary atelectasis: a pathogenic perioperative entity. *Anesthesiology.* 2005;102(4):838-54.
41. Loring SH, Butler JP. Gas exchange in body cavities. In: Farhi LE, Tenney SM, editors. *Handbook of physiology.* Bethesda: American Physiological Society; 1987. p. 283-95.
42. Joyce CJ, Baker AB, Kennedy RR. Gas uptake from an unventilated area of lung: computer model of absorption atelectasis. *J Appl Physiol.* 1993;74(3):1107-16.
43. Uzieblo M et al. Incidence and significance of lobar atelectasis in thoracic surgical patients. *Am Surg.* 2000;66(5):476-80.
44. van Kaam AH et al. Reducing atelectasis attenuates bacterial growth and translocation in experimental pneumonia. *Am J Respir Crit Care Med.* 2004;169(9):1046-53.
45. Byrd RB, Burns JR. Cough dynamics in the post-thoracotomy state. *Chest.* 1975;67(6):654-7.
46. Meyers JR et al. Changes in functional residual capacity of the lung after operation. *Arch Surg.* 1975;110(5):576-83.
47. Shapiro BA, Peruzzi WT. Respiratory care. In: Miller RD, editor. *Anesthesia.* New York: Churchill-Livingstone. 2004;2407.
48. Bastin R et al. Incentive spirometry performance. A reliable indicator of pulmonary function in the early postoperative period after lobectomy? *Chest.* 1997;111(3):559-63.
49. Overend TJ et al. The effect of incentive spirometry on postoperative pulmonary complications: a systematic review. *Chest.* 2001;120(3):971-8.
50. Freitas ER et al. Incentive spirometry for preventing pulmonary complications after coronary artery bypass graft. *Cochrane Database Syst Rev.* 2007;3:4466.
51. Guimaraes MM et al. Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. *Cochrane Database Syst Rev.* 2009;3:6058.
52. Gosselink R et al. Incentive spirometry does not enhance recovery after thoracic surgery. *Crit Care Med.* 2000;28(3):679-83.
53. Stock MC et al. Prevention of postoperative pulmonary complications with CPAP, incentive spirometry, and conservative therapy. *Chest.* 1985;87(2):151-7.
54. Ferreyra GP et al. Continuous positive airway pressure for treatment of respiratory complications after abdominal surgery: a systematic review and meta-analysis. *Ann Surg.* 2008;247(4):617-26.
55. Tobias JD. Noninvasive ventilation using bilevel positive airway pressure to treat impending respiratory failure in the post-anesthesia care unit. *J Clin Anesth.* 2000;12(5):409-12.
56. Yamazaki S et al. Intrapleural cough pressure in patients after thoracotomy. *J Thorac Cardiovasc Surg.* 1980;80(4):600-4.
57. Rodgers A et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ.* 2000;321(7275):1493.
58. Mourisse J et al. Epidural bupivacaine, sufentanil or the combination for post-thoracotomy pain. *Acta Anaesthesiol Scand.* 1992;36(1):70-4.
59. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy – a systematic review and meta-analysis of randomized trials. *Br J Anaesth.* 2006;96(4):418-26.
60. Pepe PE, Marini JJ. Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction: the auto-PEEP effect. *Am Rev Respir Dis.* 1982;126(1):166-70.
61. Tashkin DP, Cooper CB. The role of long-acting bronchodilators in the management of stable COPD. *Chest.* 2004;125(1):249-59.
62. Wise RA, Tashkin DP. Optimizing treatment of chronic obstructive pulmonary disease: an assessment of current therapies. *Am J Med.* 2007;120(8 Suppl 1):S4-13.
63. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J.* 2004;23(6):932-46.
64. Slattery DM et al. Bronchoscopically administered recombinant human DNase for lobar atelectasis in cystic fibrosis. *Pediatr Pulmonol.* 2001;31(5):383-8.
65. Quidacioli F et al. Use of minitracheotomy in high-risk pulmonary resection surgery. Results of a comparative study. *Minerva Chir.* 1994;49(4):315-8.
66. Issa MM et al. Prophylactic minitracheotomy in lung resections. A randomized controlled study. *J Thorac Cardiovasc Surg.* 1991;101(5):895-900.
67. Balkan ME et al. Clinical experience with minitracheotomy. *Scand J Thorac Cardiovasc Surg.* 1996;30(2):93-6.
68. Inagawa G et al. Tracheal obstruction caused by minitracheotomy. *Intensive Care Med.* 2000;26(11):1707.
69. Pue CA, Pacht ER. Complications of fiberoptic bronchoscopy at a university hospital. *Chest.* 1995;107(2):430-2.
70. Ferdinand B, Shennib H. Postoperative pneumonia. *Chest Surg Clin North America.* 1998;8(3):529-39, viii.
71. Nan DN et al. Nosocomial infection after lung surgery: incidence and risk factors. *Chest.* 2005;128(4):2647-52.
72. Luna CM et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. *Chest.* 1997;111(3):676-85.
73. Dupont H et al. Impact of appropriateness of initial antibiotic therapy on the outcome of ventilator-associated pneumonia. *Intensive Care Med.* 2001;27(2):355-62.
74. Ziomek S et al. Thromboembolism in patients undergoing thoracotomy. *Ann Thorac Surg.* 1993;56(2):223-6. discussion 227.
75. Kalweit G et al. Pulmonary embolism: a frequent cause of acute fatality after lung resection. *Eur J Cardiothorac Surg.* 1996;10(4):242-6. discussion 246-7.
76. Wood KE. Major pulmonary embolism: review of a pathophysiologic approach to the golden hour of hemodynamically significant pulmonary embolism. *Chest.* 2002;121(3):877-905.
77. Hope WW et al. Postoperative pulmonary embolism: timing, diagnosis, treatment, and outcomes. *Am J Surg.* 2007;194(6):814-8. discussion 818-9.
78. Velmahos GC et al. Spiral computed tomography for the diagnosis of pulmonary embolism in critically ill surgical patients: a comparison with pulmonary angiography. *Arch Surg.* 2001;136(5):505-11.
79. Mullins MD et al. The role of spiral volumetric computed tomography in the diagnosis of pulmonary embolism. *Arch Intern Med.* 2000;160(3):293-8.
80. van der Werff YD et al. Postpneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest.* 1997;111(5):1278-84.
81. Turnage WS, Lunn JJ. Postpneumonectomy pulmonary edema. A retrospective analysis of associated variables. *Chest.* 1993;103(6):1646-50.

82. Waller DA et al. Pulmonary endothelial permeability changes after major lung resection. *Ann Thorac Surg.* 1996;61(5):1435–40.
83. Fernandez-Perez ER et al. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. *Anesthesiology.* 2006;105(1):14–8.
84. Zeldin RA et al. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg.* 1984;87(3):359–65.
85. Parquin F et al. Post-pneumonectomy pulmonary edema: analysis and risk factors. *Eur J Cardiothorac Surg.* 1996;10(11):929–32. discussion 933.
86. Khan SU et al. Acute pulmonary edema after lung transplantation: the pulmonary reimplantation response. *Chest.* 1999;116(1): 187–94.
87. Demertzis S et al. Amelioration of lung reperfusion injury by L- and E-selectin blockade. *Eur J Cardiothorac Surg.* 1999;16(2): 174–80.
88. Marom EM et al. Reperfusion edema after lung transplantation: effect of daclizumab. *Radiology.* 2001;221(2):508–14.
89. Sharma AK et al. Protection from pulmonary ischemia-reperfusion injury by adenosine A2A receptor activation. *Respir Res.* 2009;10:58.
90. Shekar K et al. Bronchopleural fistula: an update for intensivists. *J Crit Care.* 2010;25(1):47–55.
91. Algar FJ et al. Prediction of early bronchopleural fistula after pneumonectomy: a multivariate analysis. *Ann Thorac Surg.* 2001;72(5):1662–7.
92. Travaline JM et al. Treatment of persistent pulmonary air leaks using endobronchial valves. *Chest.* 2009;136(2):355–60.
93. Ajemian MS et al. Routine fiberoptic endoscopic evaluation of swallowing following prolonged intubation: implications for management. *Arch Surg.* 2001;136(4):434–7.
94. Atkins BZ et al. Assessing oropharyngeal dysphagia after lung transplantation: altered swallowing mechanisms and increased morbidity. *J Heart Lung Transplant.* 2007;26(11):1144–8.
95. Schilling MK et al. Role of thromboxane and leukotriene B4 in patients with acute respiratory distress syndrome after oesophagectomy. *Br J Anaesth.* 1998;80(1):36–40.
96. Engle J et al. The impact of diaphragm management on prolonged ventilator support after thoracoabdominal aortic repair. *J Vasc Surg.* 1999;29(1):150–6.
97. Gattinoni L et al. Regional effects and mechanism of positive end-expiratory pressure in early adult respiratory distress syndrome. *JAMA.* 1993;269(16):2122–7.
98. Malo J, Ali J, Wood LD. How does positive end-expiratory pressure reduce intrapulmonary shunt in canine pulmonary edema? *J Appl Physiol.* 1984;57(4):1002–10.
99. Field S, Kelly SM, Macklem PT. The oxygen cost of breathing in patients with cardiorespiratory disease. *Am Rev Respir Dis.* 1982;126(1):9–13.
100. Katz JA, Marks JD. Inspiratory work with and without continuous positive airway pressure in patients with acute respiratory failure. *Anesthesiology.* 1985;63(6):598–607.
101. Jaber S, Chanques G, Jung B. Postoperative noninvasive ventilation. *Anesthesiology.* 2010;112(2):453–61.
102. Squadrone V et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. *JAMA.* 2005;293(5):589–95.
103. Kindgen-Milles D et al. Nasal-continuous positive airway pressure reduces pulmonary morbidity and length of hospital stay following thoracoabdominal aortic surgery. *Chest.* 2005;128(2):821–8.
104. Lefebvre A et al. Noninvasive ventilation for acute respiratory failure after lung resection: an observational study. *Intensive Care Med.* 2009;35(4):663–70.
105. Michelet P et al. Non-invasive ventilation for treatment of post-operative respiratory failure after oesophagectomy. *Br J Surg.* 2009;96(1):54–60.
106. Rocco M et al. Non-invasive pressure support ventilation in patients with acute respiratory failure after bilateral lung transplantation. *Intensive Care Med.* 2001;27(10):1622–6.
107. Perrin C et al. Prophylactic use of noninvasive ventilation in patients undergoing lung resectional surgery. *Respir Med.* 2007;101(7):1572–8.
108. Bernard GR et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med.* 1994;149(3 Pt 1):818–24.
109. Agarwal R et al. Is the mortality higher in the pulmonary vs the extrapulmonary ARDS? A meta analysis. *Chest.* 2008;133(6): 1463–73.
110. Kutlu CA et al. Acute lung injury and acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg.* 2000;69(2):376–80.
111. Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ARDS have decreased over time. *Chest.* 2008;133(5):1120–7.
112. Khadaroo RG, Marshall JC. ARDS and the multiple organ dysfunction syndrome. Common mechanisms of a common systemic process. *Crit Care Clin.* 2002;18(1):127–41.
113. Ferring M, Vincent JL. Is outcome from ARDS related to the severity of respiratory failure? *Eur Respir J.* 1997;10(6):1297–300.
114. Deitch EA. Multiple organ failure. Pathophysiology and potential future therapy. *Ann Surg.* 1992;216(2):117–34.
115. McHugh LG et al. Recovery of function in survivors of the acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1994;150(1):90–4.
116. Peter JV et al. Corticosteroids in the prevention and treatment of acute respiratory distress syndrome (ARDS) in adults: meta-analysis. *BMJ.* 2008;336(7651):1006–9.
117. Agarwal R et al. Do glucocorticoids decrease mortality in acute respiratory distress syndrome? A meta-analysis. *Respirology.* 2007;12(4):585–90.
118. Adhikari NK et al. Effect of nitric oxide on oxygenation and mortality in acute lung injury: systematic review and meta-analysis. *BMJ.* 2007;334(7597):779.
119. Adhikari N, Burns KE, Meade MO. Pharmacologic therapies for adults with acute lung injury and acute respiratory distress syndrome. *Cochrane Database Syst Rev.* 2004;4:CD004477.
120. Webb HH, Tierney DF. Experimental pulmonary edema due to intermittent positive pressure ventilation with high inflation pressures. Protection by positive end-expiratory pressure. *Am Rev Respir Dis.* 1974;110(5):556–65.
121. Ranieri VM et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. *JAMA.* 1999;282(1):54–61.
122. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med.* 2000;342(18):1301–8.
123. Levy MM. Optimal peep in ARDS. Changing concepts and current controversies. *Crit Care Clin.* 2002;18(1):15–33, v–vi.

124. Suter PM, Fairley B, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. *N Engl J Med.* 1975;292(6):284–9.
125. Roupie E et al. Titration of tidal volume and induced hypercapnia in acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1995;152(1):121–8.
126. Brower RG et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med.* 2004;351(4):327–36.
127. Phoenix SI et al. Does a higher positive end expiratory pressure decrease mortality in acute respiratory distress syndrome? A systematic review and meta-analysis. *Anesthesiology.* 2009;110(5):1098–105.
128. Hickling KG, Joyce C. Permissive hypercapnia in ARDS and its effect on tissue oxygenation. *Acta Anaesthesiol Scand Suppl.* 1995;107:201–8.
129. Fan E et al. Recruitment maneuvers for acute lung injury: a systematic review. *Am J Respir Crit Care Med.* 2008;178(11):1156–63.
130. McGregor M. Current concepts: pulsus paradoxus. *N Engl J Med.* 1979;301(9):480–2.
131. Biondi JW et al. The effect of incremental positive end-expiratory pressure on right ventricular hemodynamics and ejection fraction. *Anesth Analg.* 1988;67(2):144–51.
132. Sibbald WJ, Driedger AA. Right ventricular function in acute disease states: pathophysiologic considerations. *Crit Care Med.* 1983;11(5):339–45.
133. Bryan AC. Conference on the scientific basis of respiratory therapy. Pulmonary physiotherapy in the pediatric age group. Comments of a devil's advocate. *Am Rev Respir Dis.* 1974;110(6 Pt 2):143–4.
134. Pappert D et al. Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome. *Chest.* 1994;106(5):1511–6.
135. Mure M et al. Regional ventilation-perfusion distribution is more uniform in the prone position. *J Appl Physiol.* 2000;88(3):1076–83.
136. Gattinoni L et al. Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure. *Anesthesiology.* 1991;74(1):15–23.
137. Sud S et al. Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxic respiratory failure: a systematic review and meta-analysis. *CMAJ.* 2008;178(9):1153–61.
138. Esan A et al. Severe hypoxic respiratory failure: part 1 – ventilatory strategies. *Chest.* 2010;137(5):1203–16.
139. Extracorporeal Life Support Organization. Extracorporeal life support registry report (international summary). Ann Arbor: Extracorporeal Life Support Organization; 2008. p. 30.
140. Wigfield CH et al. Early institution of extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation improves outcome. *J Heart Lung Transplant.* 2007;26(4):331–8.
141. Sidebotham D et al. Extracorporeal membrane oxygenation for treating severe cardiac and respiratory disease in adults: part 1 – overview of extracorporeal membrane oxygenation. *J Cardiothorac Vasc Anesth.* 2009;23(6):886–92.
142. Auriant I et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. *Am J Respir Crit Care Med.* 2001;164(7):1231–5.
143. American Thoracic Society. Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. A consensus statement, American Thoracic Society, November 1995. *Am J Respir Crit Care Med.* 1996;153(5):1711–25.
144. Centers for Disease Control and Prevention. Monitoring hospital-acquired infections to promote patient safety – United States, 1990–1999. *MMWR Morb Mortal Wkly Rep.* 2000;49(8):149–53.
145. Chastre J, Fagon JY. Ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2002;165(7):867–903.
146. Vincent JL et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. *EPIC International Advisory Committee. JAMA.* 1995;274(8):639–44.
147. National Nosocomial Infections Surveillance System, Division of Healthcare Quality Promotion, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, US Department of Health and Human Services Atlanta, GA, USA. <http://www.cdc.gov/ncidod/dhqp/pdf/nnis/2004NNISReport.pdf>.
148. DiCocco JM, Croce MA. Ventilator-associated pneumonia: an overview. *Expert Opin Pharmacother.* 2009;10(9):1461–7.
149. Canadian Critical Care Trials Group. A randomized trial of diagnostic techniques for ventilator-associated pneumonia. *N Engl J Med.* 2006;355(25):2619–30.
150. Resar R et al. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf.* 2005;31(5):243–8.
151. Bouza E et al. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. *Chest.* 2008;134(5):938–46.
152. Kollef MH et al. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. *JAMA.* 2008;300(7):805–13.
153. Brochard L, Thille AW. What is the proper approach to liberating the weak from mechanical ventilation? *Crit Care Med.* 2009;37(10 Suppl):S410–5.
154. Esteban A et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *N Engl J Med.* 1995;332(6):345–50.
155. Brochard L et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *Am J Respir Crit Care Med.* 1994;150(4):896–903.
156. Boles JM et al. Weaning from mechanical ventilation. *Eur Respir J.* 2007;29(5):1033–56.
157. Levine S et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med.* 2008;358(13):1327–35.
158. Kress JP et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med.* 2000;342(20):1471–7.
159. Brook AD et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med.* 1999;27(12):2609–15.
160. Ostermann ME et al. Sedation in the intensive care unit: a systematic review. *JAMA.* 2000;283(11):1451–9.
161. Jacobi J et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med.* 2002;30(1):119–41.
162. Ely EW et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA.* 2004;291(14):1753–62.

163. Khamiees M et al. Predictors of extubation outcome in patients who have successfully completed a spontaneous breathing trial. *Chest*. 2001;120(4):1262–70.
164. MacIntyre NR et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest*. 2001;120(6 Suppl): 375S–95.
165. Miller RL, Cole RP. Association between reduced cuff leak volume and postextubation stridor. *Chest*. 1996;110(4):1035–40.
166. Engoren M. Evaluation of the cuff-leak test in a cardiac surgery population. *Chest*. 1999;116(4):1029–31.
167. Lin MC et al. Pulmonary mechanics in patients with prolonged mechanical ventilation requiring tracheostomy. *Anaesth Intensive Care*. 1999;27(6):581–5.
168. Rumbak MJ et al. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med*. 2004;32(8):1689–94.
169. Terragni PP et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: a randomized controlled trial. *JAMA*. 2010;303(15):1483–9.
170. Freeman BD et al. A meta-analysis of prospective trials comparing percutaneous and surgical tracheostomy in critically ill patients. *Chest*. 2000;118(5):1412–8.
171. Freeman BD et al. A prospective, randomized study comparing percutaneous with surgical tracheostomy in critically ill patients. *Crit Care Med*. 2001;29(5):926–30.
172. Wilson WC, Benumof JL. Respiratory physiology and respiratory function. In: Miller RD, editor. *Miller's anesthesia*. 6th ed. Philadelphia: Churchill Livingstone. 2005;696.

Postoperative Management: Extracorporeal Ventilatory Therapy

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Key Points

- The postoperative use of extracorporeal ventilatory support requires an interdisciplinary approach.
- For patients developing acute respiratory distress syndrome (ARDS) perioperatively with severe hypoxia ($\text{PaO}_2/\text{F}_1\text{O}_2 < 80 \text{ mmHg}$), extracorporeal membrane oxygenation (ECMO) therapy is appropriate if the organ failure is thought to be reversible with therapy and rest during ECMO. Recent data showed an outcome benefit for patients with ARDS and ECMO therapy as compared to ARDS without ECMO therapy.
- In the case of ARDS with $\text{PaO}_2/\text{F}_1\text{O}_2 > 80 \text{ mmHg}$ and severe hypercapnia ($\text{PaCO}_2 > 70 \text{ mmHg}$), interventional lung assist (iLA) therapy might be indicated to allow the institution of lung protective ventilation strategies. However, it should be taken into consideration that no outcome data are available for this approach.
- ECMO therapy is associated with a risk of intracranial hemorrhage. Episodes of hypoxemia before ECMO might predispose for hemorrhage. Daily sedation vacation and daily-defined sedation scales should be considered in order to detect early neurological deficits. Deep sedation is not necessary for ECMO.
- After initiation of ECMO/iLA therapy, early spontaneous breathing is considered desirable as it is known to facilitate reduction of airway pressures.

Introduction

Acute lung injury (ALI) including the more hypoxic subgroup of acute respiratory distress syndrome (ARDS) is a worldwide public health problem in intensive care medicine [1, 2]. An American-European Consensus Conference (AECC) standardized definitions for ALI and ARDS in 1994 [3], both characterized by the acute onset of hypoxemia (ALI: $\text{PaO}_2/\text{fraction of inspired oxygen fraction (F}_1\text{O}_2) < 300$, ARDS: $\text{PaO}_2/\text{F}_1\text{O}_2 < 200 \text{ mmHg}$) with radiographic infiltrates consistent with pulmonary permeability edema that occur in the absence of other identifiable causes, e.g., left heart failure [3, 4].

Despite major advances in thoracic surgery, intraoperative anesthetic management and perioperative care over the past 30 years, ALI and ARDS are responsible for the vast majority of respiratory-related deaths after thoracic surgery. There has been reported an overall prevalence rate of 2.2–4.2% post-thoracotomy ALI/ARDS in patients undergoing lung resection [5, 6]. Currently, the reported mortality rates following lung resection range from 4 to 9% after pneumonectomy and from 1 to 3% after lobectomy [6]. The causes of both mortality and morbidity following lung resection for bronchogenic carcinoma are classified as cardiac, pulmonary embolic, and respiratory complications. Respiratory complications after thoracic surgery include acute respiratory failure, noncardiogenic pulmonary edema, postperfusion lung, ARDS, and postpneumonectomy pulmonary edema [7–11]. It was

therefore agreed that the term ALI/ARDS should be employed to indicate any form of respiratory failure occurring after thoracic surgery associated with radiogenic pulmonary infiltrates in the absence of left ventricular failure [5].

Furthermore, ruptures or fistulas of the bronchial tree after pulmonary surgery, e.g., lobectomy have been reported with an incidence of 1.5–28% [12]. Inflammatory diseases seem to be an important risk factor for the development of bronchial fistulas, especially in mechanically ventilated patients [12]. Positive-pressure ventilation results in a considerable risk, in patients with bronchopleural fistula, of perpetuating the bronchial fistula and compromising surgical repair [13, 14]. Mortality has been reported to be as high as 67% in patients with bronchial fistulae receiving mechanical ventilation [12]. Therefore mechanical ventilation, applying positive airway pressures, should be avoided whenever possible, and early extubation is a major goal in the perioperative therapy [13, 14].

The pathogenesis of ALI/ARDS implies a multiple-hit sequence of various triggering factors, which results in endothelial inflammatory response (e.g., oxidative stress and surgery-induced inflammation) in addition to injurious ventilatory settings (ventilator-associated lung injury, VALI [15, 16]). A number of factors have been identified to explain and/or predict the occurrence of ALI/ARDS following lung resection. Among others, there were sex, genetic predisposition age, impaired lymphatic drainage, perioperative fluid overload (>2,000 mL intraoperatively or >3,000 mL postoperatively), surgical manipulation of the lung, prolonged one-lung ventilation, preoperative lung function, preoperative radiotherapy, or chemotherapy [5, 7, 10, 11].

Knowledge of the perioperative risk factors of major complications and understanding of the mechanisms of post-thoracotomy ALI/ARDS enable anesthesiologists to implement “protective” ventilatory lung strategies to avoid VALI. However, if these conservative therapeutical strategies are not successful, extracorporeal lung protective strategies might be indicated. This chapter reviews the background, techniques, and therapy algorithm of extracorporeal ventilatory therapy in case of ALI/ARDS in the perioperative setting of thoracic surgery.

Lung Ventilatory Protective Strategy

Significance of Extracorporeal Ventilatory Therapy

The concept of “lung protective ventilation” includes the use of low-tidal volumes, positive expiratory pressure (PEEP) and limitation of the maximum inspiratory pressure [13, 15–22]. Moreover, a post hoc analysis of the ARDS network study has indicated the existence of a clear correlation between positive inspiratory pressure and mortality: the lower the level of maximum inspiratory pressure, the better the patients outcome [19]. The reduced oxygenation usually requires high end-expiratory pressure which limits carbon dioxide elimination and

further contributes to VALI [20]. Therefore, in ALI/ARDS the implementation of such lung-protective concepts is frequently limited by a therapeutic dilemma: with the use of lung-protective ventilation, the risk of severe hypercapnia increases. Although, the effects of the resultant hypercapnia have not yet been conclusively clarified, hypercapnia, e.g., results in pulmonary and cardiac vasoconstriction, peripheral arterial and cerebral vasodilation, increased cardiac output, delivery from catecholamines, reduction of renal perfusion and triggers respiratory drive. These adverse pathophysiologic consequences could result in organ damage as myocardial insufficiency, renal failure or restriction of liver/intestine circulation due to systemic hypercapnia.

In such cases of severe hypoxemia or hypercapnia, the management of ALI/ARDS requires specific therapeutic measures including techniques of extracorporeal lung ventilatory support. In patients suffering from severe ARDS with life-threatening hypoxemia, a pump-driven veno-venous (VV) extracorporeal membrane oxygenation (ECMO) has been used. Recently, a pumpless extracorporeal lung support system was developed using an arterio-venous bypass, into which a gas exchange membrane is integrated (pumpless interventional lung assist [iLA]). iLA provides effective CO₂ elimination but only a moderate improvement in oxygenation.

The decoupling of ventilation and oxygenation allows for several ventilation strategies: All strategies have sufficient PEEP level in common to achieve an almost complete recruitment of the lung at a minimal pressure amplitude. Whether continuous positive airway pressure (CPAP) with spontaneous breathing, bi-level positive airway pressure (BIPAP) with a low respiratory frequency and a reduced peak airway pressure, or high frequency oscillation ventilation is applied should be decided for each individual case [21, 22].

History of Extracorporeal Ventilatory Therapy

Bioengineering, physiology, and pharmacology converge in the intensive care unit. Mechanical devices for monitoring and treatment are essential for the application of physiologic principles and management. Extracorporeal circulation is the ultimate example of this complex interaction.

Cardiopulmonary bypass technology was developed to provide circulatory and respiratory support during cardiac surgery. In 1960s and 1970s, a number of creative physicians conceived the possibility of employing this technology to support patients with life-threatening cardiac or respiratory failure. The challenge was to provide extracorporeal circulation for a period sufficiently long (i.e., days or weeks) to allow intrinsic healing of the diseased heart and lungs. The various systems that provide long-term extracorporeal life support are known collectively as ECMO. When used with extra-thoracic cannulation for respiratory support the technique is called ECMO. The modern era of ECMO for adults with ARDS was pioneered by Bartlett and colleagues in 1972 [23]. Their results and those at other institutions showed that ECMO could be applied with encouraging survival, exceeding 50% [24–27].

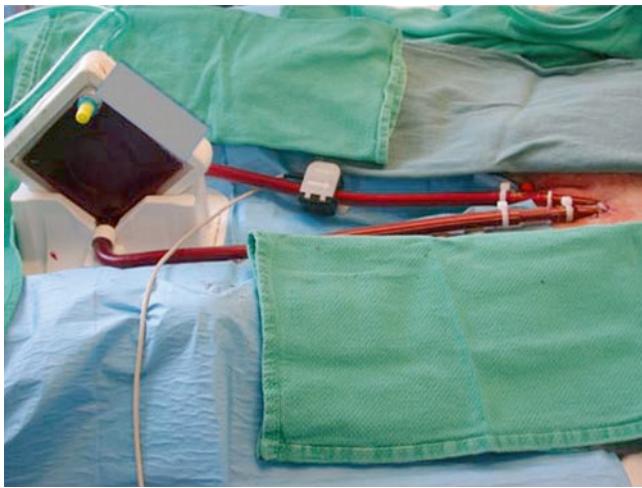


FIG. 43.1. The iLA device is shown between a patient's legs during placement with femoral cannulations. The patient's body is to the right, out of the photograph. The inflow to the device is from the femoral artery (near cannula) and the return is via the femoral vein (far cannula).

In a recent, multicenter randomized controlled trial, in which the conventional ventilation was compared to ECMO therapy for severe ARDS (CESAR trial), ECMO demonstrated a survival benefit at 6 months [28].

iLA was firstly described by Pott and colleagues [29] in 1951. They investigated an experimental approach to maintain pulmonary function by an extracorporeally connected homologous lung in a large animal model. In addition, Rashkind et al. [30] constructed a bubble oxygenator for extracorporeal lung support in a child in 1965, creating a shunt between the femoral vein and artery to eliminate CO_2 . Even though this early approach failed due to clotting, the new concept of iLA was born. Over the last 40 years, experimental and clinical work has been performed to improve the field of extracorporeal lung assist. In 1999, the iLA as the first pumpless mode for CO_2 removal was developed and applied in a patient [31]. The iLA became commercially available in 2001 and was called Nova Breath® (Josta Medizintechnik, Hirrlingen, Germany); since 2002 it has been called Novalung® (Novalung GmbH, Hechingen, Germany) (see Fig. 43.1).

Extracorporeal Membrane Oxygenation (ECMO)

Indications

In terms of respiratory failure in adults, the most common indication for ECMO is due to life-threatening hypoxemia caused by pneumonia, severe lung contusion in trauma patients [32, 33], bronchopleural fistulas after lung resection [14], lung transplantation as well as primary graft failure in order to prevent ventilator-induced lung injury and to reduce inspira-

TABLE 43.1. Treatment algorithm for ALI/ARDS.

Conservative therapy according
Ventilator settings (pressure-controlled or volume-controlled ventilation)
• PEEP $10-15 \pm 2 \text{ cmH}_2\text{O}$
• Inspiratory peak pressure (PIP) $< 35 \text{ cmH}_2\text{O}$
• Tidal volume (Vt): 4–6 mL/kg
• Respiratory rate (RR): 15–20 breaths/min
Basic treatment approach
• Lung protective ventilation strategy
• Sufficient oxygenation ($\text{SpO}_2 > 90\%$)
• Lung edema reduction, fluid restriction, <i>application of PEEP as high as possible depending on the surgical intervention</i>
• Prevention/treatment MODS
• Empirical antibiotic treatment
• <i>Prone position: 6 ± 2 h</i>
• Nitric oxide administration (initially 10–40 ppm)
In case of pulmonary hypertension (mean pulmonary arterial pressure (PAPm) $> 25 \text{ mmHg}$ or right ventricular failure (TEE) or $\text{PaO}_2/\text{F}_1\text{O}_2 < 200$
If <i>RESPONSE</i> : $\Delta \text{PAPm} > -3 \text{ mmHg}$, or $\Delta \text{paO}_2/\text{F}_1\text{O}_2 > +15\%$ or $\Delta \text{QsQt} > -5\%$, continuation of NO administration, if <i>NO RESPONSE</i> , discontinuation of NO administration

Adapted from Refs. [25, 76, 77]

TABLE 43.2. Criteria for ECMO indication, fast-entry and weaning.

ECMO indication (first 24 h): $\text{PaO}_2/\text{F}_1\text{O}_2 < 80 \text{ mmHg} + \text{PIP} > 35 \text{ cmH}_2\text{O}$
ECMO indication (>24 h after initial treatment)
$\text{PaO}_2/\text{F}_1\text{O}_2 < 80 \text{ mmHg} + \text{PIP} > 32 \text{ cmH}_2\text{O}$
Fast-entry ECMO: $\text{PaO}_2/\text{F}_1\text{O}_2 < 50 \text{ mmHg} + \text{PIP} > 35 \text{ cmH}_2\text{O} > 2 \text{ h}$
Weaning of ECMO/main criteria
$\text{F}_1\text{O}_2 < 0.4$
$\text{PaO}_2 > 80 \text{ mmHg}$
Target ventilator settings
BIPAP: $\text{PEEP} \pm 12 \text{ cmH}_2\text{O}$, $\text{PIP} < 30 \text{ cmH}_2\text{O}$, $\text{Vt}: 4-6 \text{ mL/kg}$
RR spontaneous ~5 breaths/min
Procedure
Reducing blood flow 0.5 L/min every 12 h to minimal blood flow of 0.5–1.0 L/min
$\text{PaCO}_2 < 60 \text{ mmHg}$, reducing gas flow and F_1O_2 over membrane
ECMO trial off: gas flow 0.5–1 L/min over 15 min, criteria fulfilled: discontinue ECMO

Adapted from Refs. [25, 76]

tory peak pressures (see Tables 43.1 and 43.2, Figs 43.2 and 43.3). Respiratory complications remain a major cause of morbidity and mortality of lung surgery [34]. While the overall incidence of such complications can be as high as 15%, bronchopleural fistulas are fortunately uncommon. Most cases of bronchopleural fistulas occur early after surgery, are difficult to treat and are associated with a high mortality [35]. Achieving adequate ventilation is often difficult in these patients, particularly if single-lung ventilation has to be achieved [35]. The use of differential ventilation using a double-lumen endotracheal tube and jet ventilation have been the traditional options [36]. The use of VV ECMO is an alternative therapeutic option as bridge for successful surgical repair of bronchopleural fistulas and for managing patients with primary graft failure after lung transplantation [35, 36].

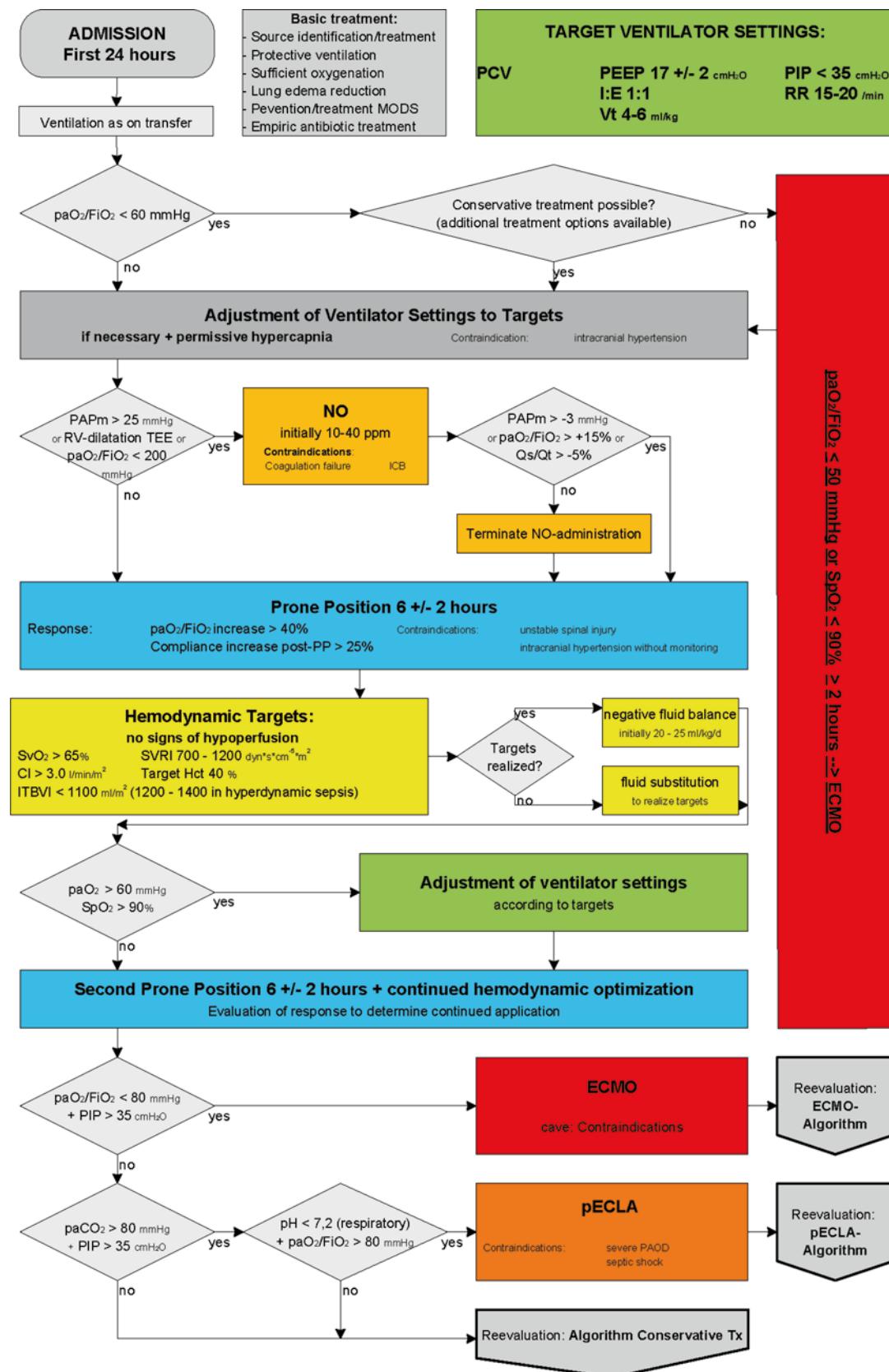


FIG. 43.2. Treatment algorithm for ALI/ARDS. In case of deterioration of oxygenation or development of severe hypercapnia with right heart failure within 2 h after initiation of the conservative treatment, an extracorporeal lung assist device (ECMO/iLA) should be considered in order to avoid secondary lung damage (barotrauma, volutrauma, pneumothorax, bronchopleural fistula) due to the ventilatory settings and to prevent consecutive organ failure (heart, circulation, renal, liver failure). (Deja et al. [76], with kind permission from Field House publishing.)

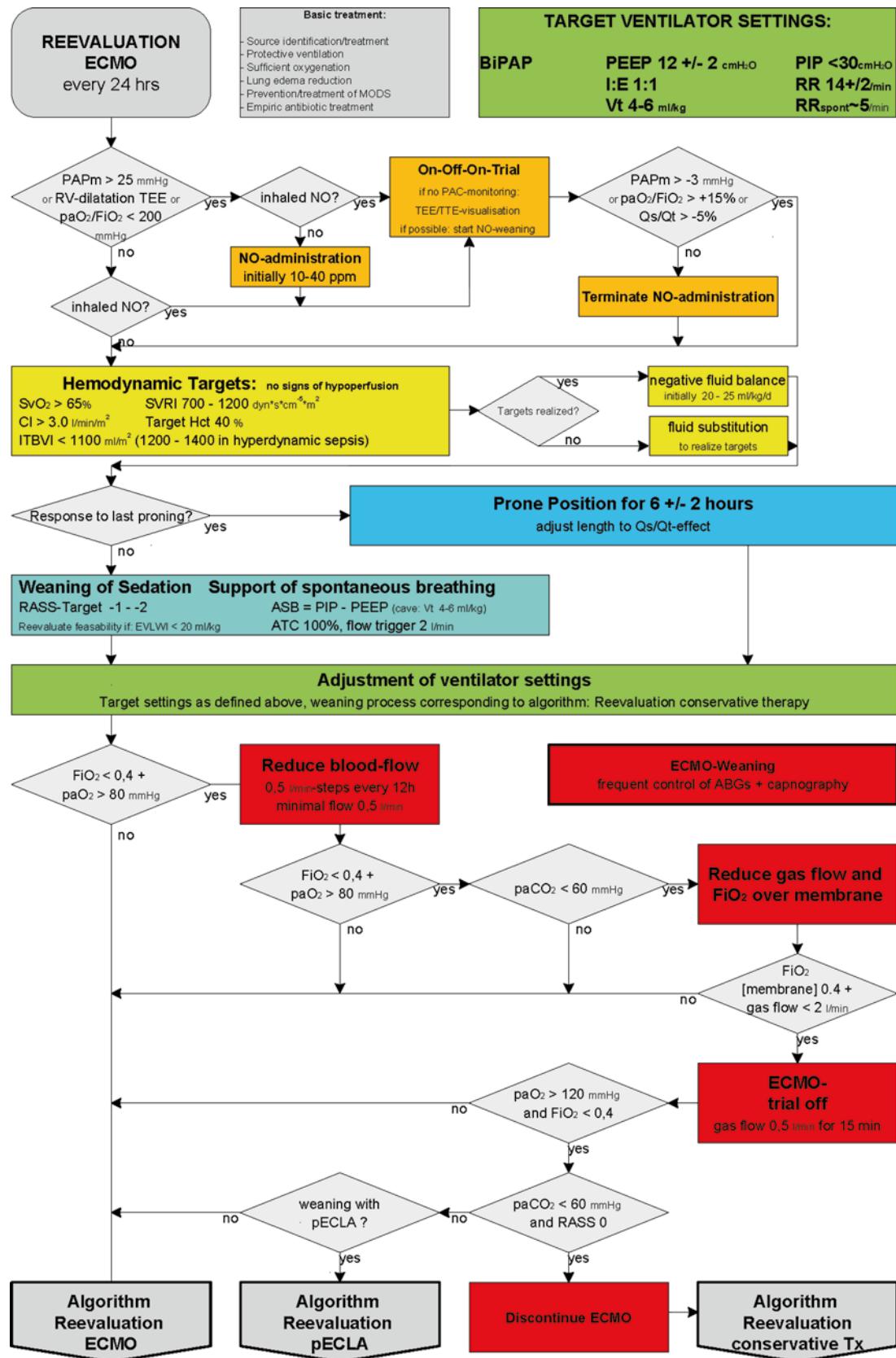


FIG. 43.3. Criteria for ECMO indication, fast-entry and weaning (Deja et al. [76], with kind permission from Field House publishing.)

However, to institute ECMO, several factors should be taken into consideration. The institution of ECMO is appropriate if the organ failure is thought to be reversible with therapy and rest on ECMO. If underlying lung pathology does not recover, ECMO might be instituted as bridging for transplant [37].

Technical Aspects of ECMO

ECMO can be inserted in a VV configuration which provides oxygenation (in case of respiratory failure not responding to mechanical ventilation) or can be used as veno-arterial (VA) configuration (providing both respiratory and cardiac support). ECMO implies the diversion of blood from a major systemic vessel through a gas exchange device (membrane oxygenator) and back to a major blood vessel. The term VV-ECMO refers to blood being drained from the venous system and returned to the venous system [37].

For VV perfusion, flow is initiated at 10–15 mL/kg/min and advanced over 10–15 min to a maximum of 100–150 mL/kg/min. Flow is then decreased, watching the patient's pulse oximeter until the optimal flow for oxygenation is observed. This would be from 25 to 75% of the cardiac output providing sufficient oxygenation. For low extracorporeal blood flow (about 3 L/min), two cannulae are sufficient. But in case of increased cardiac output, a second oxygenator and blood pump with three cannulae are often used to achieve sufficient gas exchange [37, 38]. Membrane oxygenators are used in combination with a pump to supply up to 5–7 L/min support. Recently, new, improved pumps, with coated circuits, have reduced the risk of hemolysis caused by centrifugal pumps [39, 40]. Moreover, plasma-leakage-resistant oxygenators have enabled the safe use of ECMO for much longer periods of time up to 59 days without changing the oxygenator [39, 41]. ECMO flow depends on volume load and will drop with hypovolemia or cannula malposition, but hypervolemia is not necessary and

could be harmful by increasing lung edema. Hypovolemia usually manifests as negative pressure upstream to the blood pump. "Kicking" or "chatter" of the venous tubing as well as a drop of the cardiac output visualized low volume load [37]. A slight reduction in flow may be helpful.

In the last two decades, cannulae have improved flow dynamics allowing percutaneous insertion with the Seldinger technique into femoral and jugular vessels which is the standard technique of most of the ARDS centers [38]. Percutaneous insertion is associated with less bleeding complication as well as a lower risk of infection. In order to facilitate this high flow, the placement of large catheters is required into the circulation. For adults, the intravascular catheters may be 20 French or larger. The cannulae are usually heparin- or "bio"-coated in order to reduce the risk of clot formation. In case of successful weaning of ECMO, the patient is decannulated usually without surgical intervention [38].

The primary advantage to VV ECMO is that it avoids cannulation and ligation of a major artery which is associated with a greater risk of thromboembolism including air embolism. Furthermore, Hemilla and colleagues demonstrated an improved survival to discharge benefit in patients with VV ECMO (59.5%), VA changed to VV (73.3%) compared to VA ECMO (31.9%) and VV changed to VA (14.8%) [26]. Even in case of severe ARDS without right heart failure, the preferred regimen is VV-ECMO. There are different types of VV-ECMO depending on the cannulation sites [37]:

A: Jugular to femoral

B: Femoral to femoral

C: Double-lumen in the internal jugular vein. Blood is withdrawn from the inferior vena cava through one port, circulated through the membrane oxygenator and returned to the right atrium through a second port in the same double-lumen catheter. This minimizes recirculation (see Fig. 43.4).

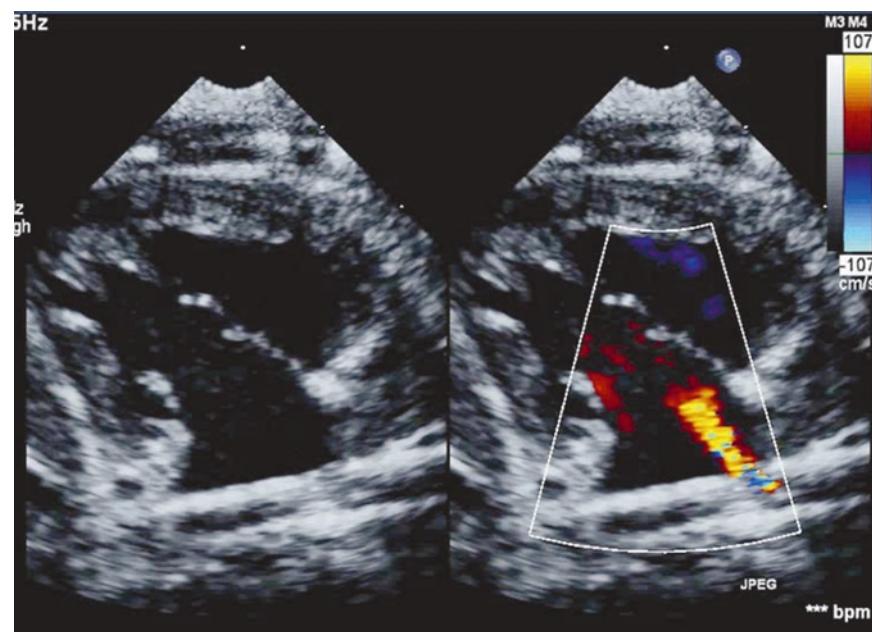


FIG. 43.4. Bicaval transesophageal echocardiography (TEE) views (left black and white, right color-flow doppler) of a double-lumen ECMO cannula which has been placed via the right internal jugular vein and the superior vena cava (bottom right of pictures). The venous inflow to the ECMO is from the distal lumen of the cannula which is positioned in the inferior vena cava (bottom left of the pictures). The oxygenated blood is returned by the proximal lumen. The return orifice of the proximal lumen is positioned with TEE so that the return flow (yellow jet in doppler picture) is directed toward the tricuspid valve (center of pictures). (Photo courtesy of Avalon Laboratories, LLC. Grand Rapids MI.)

From a gas exchange point of view, hypoxia is treated by increasing both the ECMO flow rate and F_1O_2 of the ECMO circuit, not by altering the F_1O_2 and PEEP on the ventilator [37]. Attempts should be made to wean the F_1O_2 on the ventilator and maintain a lung protective strategy with low plateau pressures, low tidal volumes, and adequate PEEP.

Elimination rate of CO_2 depends on gas flow over the membrane. Gas flows up to 15 L/min are necessary in patients without CO_2 elimination by the lungs. CO_2 control should be made via the ECMO gas flow through the membrane, not by altering the respiratory rate on the ventilator to avoid further VALI.

Temperature Management on ECMO

Because heat is lost through the evaporation of water as blood flows through the artificial lung, it is often necessary to warm the patient on ECMO. Although normothermia can be maintained through use of external warming devices, it is usually more efficient to warm the extracorporeal blood before infusion. In most ECMO centers, heat exchangers are routinely used. At times the heat exchanger may also be used to cool the patient to a preset temperature in order to effect a decrease in oxygen consumption. The heat exchanger should be placed in-line after the artificial lung during ECMO in order to optimize the efficiency of the device.

Monitoring for Anticoagulation

ECMO patients require only a low level of systemic anticoagulation to prevent clotting of the cannulae, tubing and oxygenator because current devices are coated with heparin. The level of systemic heparinization required is not definitely known, although an activated partial thromboplastin time (APTT) of 50–70 s and a platelet count $>80 \times 10^9/L$ is reasonable [42]. In high flow systems of about 4–7 L/min, an APTT above 50 s is sufficient to prevent clotting. Regular measurement of clotting profile, platelet count, and hemoglobin should be performed as least twice per day.

Hemolysis is another well-recognized complication of ECMO with an incidence of 5 and 8% and should be routinely monitored [42]. This is done by regular (daily) checking of the plasma-free hemoglobin and haptoglobin.

In case of heparin-induced thrombocytopenia (HIT), argatroban seems to be an adequate alternative for anticoagulation during ECMO [43].

Complications Associated with ECMO Therapy

Bleeding Complication and Thrombosis

The most common complications associated with ECMO are life-threatening thrombosis and excessive bleeding caused by coagulopathy [42–45]. Continuous activation of the contact and fibrinolytic systems by the circuit as well as consumption and dilution of factors occurs within minutes of initiation

of ECMO [46]. Platelets adhere to surface fibrinogen and are activated. As a consequence, platelet aggregation and causes platelet count drop [47, 48]. Correction by platelet transfusion produces only a temporary increase [48]. Prolonged duration of ECMO exacerbates these negative effects [48]. Heparin-coated circuits have been reported to reduce cell trauma [49] as well as complement [50] and granulocyte [51] activation. However, systemic heparinization is still advisable because of the risk of end-organ damage from microthrombus and fibrin deposition, although the level of heparinization required is still under debate [42]. Macroscopic clots cause a variety of thromboembolic events in patients considered adequately anticoagulated [52]. Furthermore, Lidegran and colleagues [53] reported intracranial lesions (bleeding, infarction) within the first 7 days after ECMO initiation in 45/123 (37%) of patients.

Cerebral Hemorrhage/Infarction

The use of ECMO in acute respiratory or cardiac failure increases survival, but may at the same time cause damage to the brain [54]. The major cause of death in ECMO-treated patients is not due to irreversible pulmonary or heart failure but to cerebral injury caused by intracranial hemorrhage or infarction [53, 55].

Changes in cerebral blood flow and the use of heparin may contribute to both hemorrhagic and nonhemorrhagic intracranial lesions. ECMO survivors carry a high risk of brain injury and subsequent functional deficit [56]. Hypoxia is thought to be one of the most important factors in developing cerebral injury [57, 58]. The brain responds to hypoxia by increasing cerebral oxygen transport and cerebral oxygen extraction. A mild degree of hypoxia can be tolerated. However, prolonged periods of severe hypoxia may result in a loss of ability of the brain to maintain adequate oxygen transport and cerebral oxygen metabolism, leading to irreversible brain injury [59]. ARDS patients may suffer from hypoxia for hours to days before ECMO therapy is initiated [58].

In addition, ECMO therapy itself can cause cerebral injury [58]. When patients are cannulated for ECMO, there is a period of hypoxia before and during cannulation [58, 60]. The cannulation itself, together with creation of solid and gaseous microemboli during perfusion, may cause cerebral injury. Arterial emboli may occur in connection with retrograde arterial cannulation [60, 61]. Even careful cannulation with the Seldinger technique may cause thrombus formation.

Cerebral auto-regulation is an important homeostatic mechanism that maintains cerebral blood flow over a wide range of cerebral perfusion pressures. Systemic insults and hypoxia can disrupt cerebral auto-regulation, leaving the cerebral microcirculation vulnerable to changes in systemic blood pressure. Hypotension can result in ischemic cerebral damage and hypertension can cause cerebral hyperemia and increase the risk of cerebral hemorrhage [62]. Loss of auto-regulation in an already injured brain, combined with systemic heparin therapy, can cause cerebral hemorrhage [63]. During VA

ECMO, cerebral perfusion is mainly nonpulsatile which may lead to diffuse brain edema [64]. The risk is reduced in VV-ECMO, in which the cerebral perfusion is pulsatile [64].

Pumpless Interventional Lung Assist (iLA)

Indications

There are two major indications for extracorporeal ventilation. It can be applied to give the injured or diseased lung a chance to heal (bridge to recovery) or in an end-stage lung disease, it might be used as a bridge to lung transplantation (see Tables 43.1 and 43.3, Figs 43.2 and 43.5) [65–69].

The use of iLA in addition to lung protective ventilation has been reported in one center to have a high survival rate (84%) in a series patients with severe post lung-resection ARDS [70]. The iLA device has also been used as a “bridge to transplant” in patients with pulmonary hypertension [67, 68, 71]. In this context, the device has been implanted with main pulmonary artery and vein cannulations during sternotomy (see Fig. 43.6). It has been possible to wean several patients with ventilatory and right-heart failure from iLA and positive pressure ventilation while waiting for lung transplantation (see Fig. 43.7).

The iLA can be used for CO_2 removal in cases of severe hypercapnia and respiratory acidosis in order to avoid the injury of mechanical ventilatory support. Bein et al. [65] studied, in a single-center study, 90 patients with ARDS supported with the pumpless iLA and reported a survival rate (weaning of iLA) of 41%. The iLA has been used in patients with broncho-pleural fistulas after lung surgery [14], chest trauma patients (lung contusion) [66], in patients with blast injury in the war zone or as a bridge to lung transplant [67, 68].

However, apart from these small randomized studies and case reports, no outcome data are currently available.

TABLE 43.3. Criteria for iLA indication, weaning iLA.

iLA indication (first 24 h)
$\text{PaCO}_2 > 80 \text{ mmHg} + \text{PIP} > 35 \text{ cmH}_2\text{O} + \text{pH} < 7.2 \text{ (respiratory)} + \text{PaO}_2 / \text{F}_1\text{O}_2 > 80 \text{ mmHg}$
iLA indication (>24 h after initial treatment)
$\text{PaCO}_2 > 80 \text{ mmHg} + \text{PIP} > 32 \text{ cmH}_2\text{O} + \text{pH} < 7.2 \text{ (respiratory)} + \text{PaO}_2 / \text{F}_1\text{O}_2 > 80 \text{ mmHg}$
Weaning of iLA/main criteria
Ramsay sedation score (RASS) 0/–1
$\text{F}_1\text{O}_2 < 0.4$
$\text{PaCO}_2 < 60 \text{ mmHg}$
Target ventilator settings
BIPAP: $\text{PEEP} \pm 12 \text{ cmH}_2\text{O}$, $\text{PIP} < 30 \text{ cmH}_2\text{O}$, Vt: 4–6 mL/kg , $\text{RR } 14 \pm 2 \text{ breaths/min}$, $\text{RR spontaneous } \sim 5 \text{ breaths/min}$
Procedure
Reducing O_2 flow iLA in steps of 11/min
iLA O_2 -flow <2 L/min: iLA 6 h without gas flow
iLA trial off: criteria fulfilled: discontinue iLA

Adapted from Ref. [76]

Technical Aspects of iLA

The iLA device is a pumpless arterio-venous shunt with carbon dioxide elimination as primary function owing to the arterial inflow blood. The principle is simple diffusion. Blood flows over the exterior surface (1.5 m^2) of the device fibers and the ventilating gas (O_2 sweep) flows inside these fibers. The iLA consists of a plastic gas exchange module with diffusion membranes made from polymethylpentene (PMP). The PMP fibers are woven into a complex configuration of hollow fibers. Gas transfer takes place without direct contact with blood. In addition, the blood-contacting PMP membrane surface is treated with a heparin coating to provide a biocompatible and nonthrombogenic surface [31].

The iLA is a low pressure-gradient device designed to operate without a mechanical pump. Based on this principle, adequate mean arterial blood pressure is mandatory. The preferred access sites are the femoral vessels by percutaneous cannulation using Seldinger's technique (see Fig. 43.1). Used in this configuration, usually about 20% of the cardiac output (1–2 L/min) runs through the iLA, driven by the left ventricle, and mixes with the remaining 80% of the cardiac output in the venous vasculature. One limitation of this device is that patients with primarily an oxygenation disorder may not benefit sufficiently from the pumpless iLA mode in terms of oxygenation, however carbon dioxide elimination is usually not a problem.

The blood enters the device through the inlet connector. The blood flows into the blood distributing chamber. Any microsized air bubbles that may have entered the device are removed through the de-airing ports. The blood flows into the main chamber where gas exchange takes place. The oxygen and CO_2 -depleted blood is returned to the patient via the blood outflow [67]. Two de-airing membranes are integrated at the top apex on both sides of the device. These de-airing membranes allow gas bubbles but not liquids to cross. In addition, they facilitate priming and de-airing of the device and are also used to eliminate any air trapped in the device during support. An oxygen supply is connected to the gas inflow connector, the lower gas outflow connector is open to the atmosphere and is the site where gas is exhausted from the device [68, 69].

Complications Associated with iLA Therapy

Ischemic complications of the lower limb were reported to be associated with the large cannulation size for the arterial cannulation (17 French) initially used for iLA [65]. As smaller cannulae (13 and 15 F) have become available, the ischemic complication rate has markedly decreased. It is not recommended to use 17 F cannulae for femoral arterial cannulation. Advantages of iLA are: avoiding all the complications related to a mechanical pump, reduced blood-contact surfaces, and relatively easy clinical management. Disadvantages are the indirect control of blood flow which is the result of the arterio-venous pressure gradient and the limited oxygen transfer capacity.

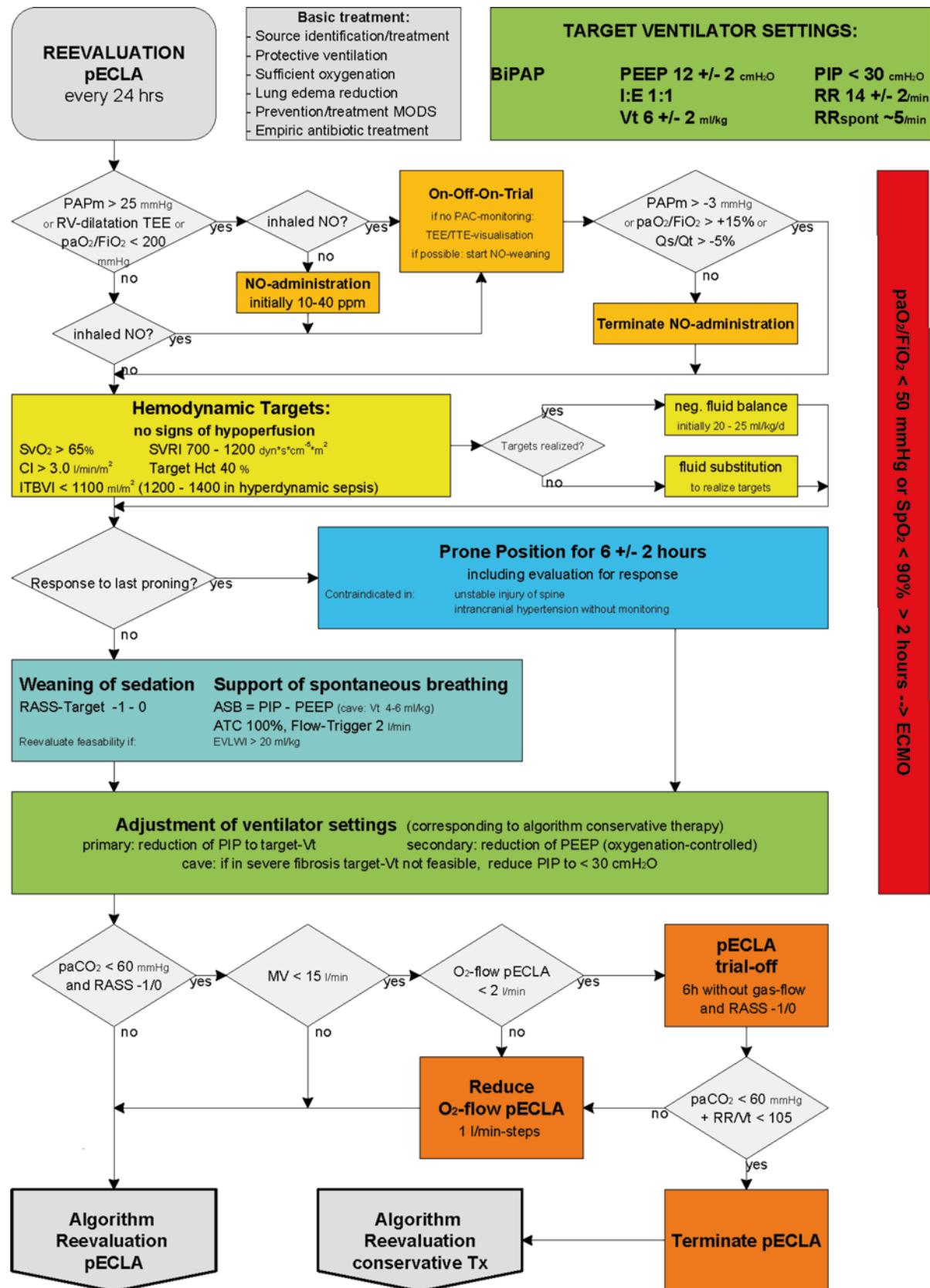


FIG. 43.5. (Criteria for iLA indication, weaning iLA according to Deja et al. [76], with kind permission from Field House publishing).

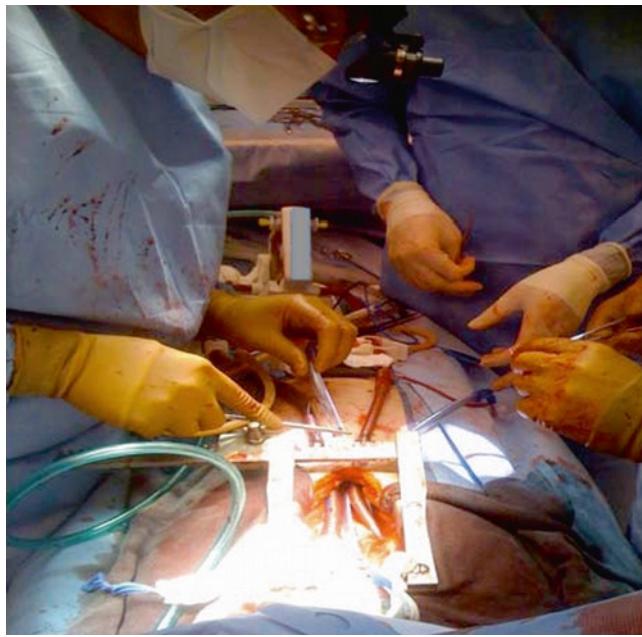


FIG. 43.6. Intra-thoracic implantation of interventional lung assist cannulae during sternotomy in a patient with pulmonary hypertension, seen from Anesthesiologist's perspective. The iLA device can be seen between the patient's legs. The inflow cannula to the device is on the *left side* of the incision, placed into the main pulmonary artery. The return cannula, to the *right*, is into the right upper pulmonary vein. The surgeon is placing a mediastinal drain between the cannulae prior to closing the incision.



FIG. 43.7. A patient with pulmonary hypertension has been weaned from ECMO and mechanical ventilation with a trans-thoracic implantation of an iLA device. The device can be seen on the side of the patient's bed.

Multimodal Therapeutic Approach

Weaning of Sedation

Daily interruption of sedative drug infusions significantly reduced the duration of mechanical ventilation and the length of stay in the intensive care unit [72, 73]. This should be

considered in patients requiring extracorporeal ventilatory support. Moreover, it is important with respect to the early detection of new neurological deficits caused by cerebral infarction or hemorrhage. Therefore, daily assessment of the level of sedation is recommended in order to prevent oversedation [73].

Early Spontaneous Breathing

Spontaneous breathing as a part of a “lung protective strategy” by decreasing intrapulmonary shunt and intra-thoracic pressures, as well as improving organ perfusion should be achieved as early as possible [74, 75]. Furthermore, after thoracic surgery this is beneficial in protecting surgical bronchial reconstruction as well as in preventing of bronchial fistulas and bronchial suture dehiscence [14, 35, 65].

Clinical Case Discussion

Case: A 17-year-old male sustained multiple trauma with a traumatic tracheal rupture (approximately 8–10 cm length on the pars membranacea) and bilateral severe lung contusions after a fall of 7 m height (Figs. 43.8 and 43.9). Tracheal rupture as well as mediastinal emphysema was diagnosed on the immediate performed CT scan. Chest tubes were inserted on both sides due to pneumothoraces. Fiberoptic bronchoscopy was immediately performed in order to position the endotracheal tube as near as possible to the carina. After this intervention, the subcutaneous emphysema decreased.



FIG. 43.8. CT scan thorax of a male patient with severe ARDS and traumatic tracheal rupture, mediastinal emphysema.

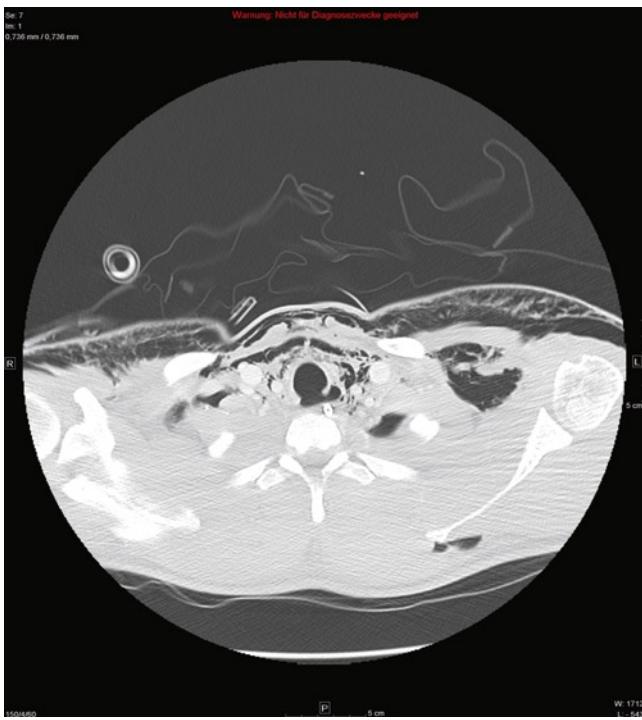


FIG. 43.9. CT scan thorax of a male patient with severe traumatic tracheal rupture, mediastinal emphysema.

However, within a few hours the patient developed severe ARDS, due to lung contusion (pressure-controlled ventilation, $\text{PaO}_2/\text{F}_1\text{O}_2$ ratio <200 , PEEP: 15, PIP: 35). Tracheal rupture affected the whole tracheal wall with protrusion of mediastinal structures into the lumen, therefore a surgical repair was indicated. The anesthesia team will need to decide if the patient will tolerate the proposed procedure and if so, then what management strategies can be used to improve the perioperative outcome.

Questions

- Will the patient tolerate the operative procedure without extracorporeal lung assist?
- What specific anesthetic considerations are related to patient's disease?
- How to plan the anesthesia and operative procedure in an interdisciplinary approach?
- What postoperative management strategies will improve patients' outcome?
- In this situation of severe ARDS ($\text{PaO}_2/\text{F}_1\text{O}_2 < 100$, PEEP: 15–17 mmHg, PIP: 35 mmHg), the patient would not tolerate the thoracic surgical procedure under one-lung ventilation without the risk of developing severe hypoxemia and hypercapnia.
- Anesthetic considerations include perioperative difficult airway management (placement of a double-lumen tube?), intraoperative hypoxia and hypercapnia during one-lung ventilation, postoperative airway management to prevent tracheal suture dehiscence.

• Preoperative Management: Conservative treatment strategy with prone positioning, restrictive volume therapy and nitric oxide administration before the surgical intervention was performed. However, oxygenation index did not increase with prone positioning. Therefore, intraoperative anesthetic management was planned as follows:

- Preoperative initiation of VV-ECMO (femoral veins on both side 23 F), 4–5 L/min blood flow
- Apneic oxygenation with PEEP: 10 mmHg; or no ventilation with full ECMO blood flow (advantage: optimal surgical conditions)
- Airway management: tracheostomy with insertion of an uncuffed tracheostomy tube
- Postoperative management:
 - Prone positioning should be considered due to lung recruitment after lung surgery if there is a clinically relevant increase in oxygenation (reevaluate every 24 h).
 - ECMO therapy in patients with ARDS improves outcome of some patients.
 - Early spontaneous breathing reduces ventilation pressures and prevents tracheal suture dehiscence.
 - Daily sedation vacation to detect, as early as possible, neurological deficits in patients with ECMO therapy.

References

1. Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med.* 2000;342:1334–49.
2. Wheeler AP, Bernard GR. Acute lung injury and the acute respiratory distress syndrome: a clinical review. *Lancet.* 2007;369:1553–64.
3. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med.* 1994;149:818–24.
4. Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med.* 2005;353:1685–93.
5. Kutlu CA, Williams EA, Evans TW, et al. Acute lung injury and acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg.* 2000;69:376–80.
6. Ruffini E, Parola A, Papalia E, et al. Frequency and mortality of acute lung injury and acute respiratory distress syndrome after pulmonary resection for bronchogenic carcinoma. *Eur J Cardiothorac Surg.* 2001;20:30–7.
7. Dulu A, Pastores S, Park B, et al. Prevalence and mortality of acute lung injury and ARDS after lung resection. *Chest.* 2006;130:73–8.
8. Zeldin RA, Normandin D, Landring D, et al. Postpneumonectomy pulmonary edema. *J Thorac Cardiovasc Surg.* 1984;87:359–65.
9. Turnage WS, Lunn JJ. Postpneumonectomy pulmonary edema. A retrospective analysis of associated variables. *Chest.* 1993;103:1646–50.
10. Jordan S, Mitchell JA, Quinlan GJ, et al. The pathogenesis of acute lung injury following pulmonary resection. *Eur Respir J.* 2000;69:376–80.
11. Williams EA, Evans TW, Goldstraw P. Acute lung injury following lung resection: is one-lung anesthesia to blame? *Thorax.* 1996;51:114–6.

12. Lois M, Noppen M. Ronchiopleural fistulas: an overview of the problem with special focus on endoscopic management. *Chest*. 2005;128:3955–65.
13. Villar J, Kacmarek RM, Perez-Mendez L, et al. A high-positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. *Crit Care Med*. 2006;34:1311–8.
14. Hommel M, Deja M, von Dossow V, et al. Bronchial fistulae in ARDS patients: management with an extracorporeal lung assist device. *Eur Respir J*. 2008;32:1652–5.
15. Frank JA, Parsons PE, Matthay MA. Pathogenetic significance of biological markers of ventilator-associated lung injury in experimental and clinical studies. *Chest*. 2006;130(6):1906–14.
16. Ranieri VM, Slutsky AS. Respiratory physiology and acute lung injury: the miracle of Lazarus. *ICM*. 1999;25(10):1040–3.
17. The Acute Respiratory distress Syndrome network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1301–8.
18. The ARDS network. Ketokonazole for early treatment of acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2000;283:1995–2002.
19. Hager ND, Krishnan JA, Douglas LH, et al. Tidal volume reduction in patients with acute lung injury when plateau pressure are not high. *AJRCCM*. 2005;172:1241–5.
20. Terragni PP, Del Sorbo L, Mascia L, et al. Tidal volume lower than 6 ml/kg enhances lung protection: role of extracorporeal carbon dioxide removal. *Anesthesiology*. 2009;111(4):826–35.
21. Steinberg KP, Hudson LD, Goodman RB, et al. National heart lung, and blood institute acute respiratory distress syndrome (ARDS) Clinical Trials Network. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. *N Engl J Med*. 2006;354:1671–84.
22. Von Mach M-A, Kaes J, Omogbehin B, et al. An update on interventional lung assist devices and their role in acute respiratory distress syndrome. *Lung*. 2006;184:169–75.
23. Bartlett RH, Burns NE, Fong SW, et al. Prolonged partial veno-arterial bypass: physiologic, biochemical and hematologic responses. *Surg Forum*. 1972;23:178–80.
24. Anderson HL, Delius RE, Sinard JM, et al. Early experience with adult extracorporeal membrane oxygenation in the modern era. *Ann Thorac Surg*. 1992;53:553–63.
25. Lewandowski K, Rossaint R, Pappert D, et al. High survival rate in 122 ARDS patients managed according to a clinical algorithm including extracorporeal membrane oxygenation. *Intensive Care Med*. 1997;23:819–35.
26. Hemilla MR, Rowe SA, Boules TN, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. *Ann Surg*. 2004;240:595–605.
27. Linden VB, Lidegran MK, Frisen G, et al. ECMO in ARDS: a long-term follow-up study regarding pulmonary morphology and function and health-related quality of life. *Acta Anaesthesiol Scand*. 2009;53:489–95.
28. Peek GJ, Mugford M, Tiruvoipati R, et al. CESAR trial collaboration. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*. 2009;7(374):1351–63.
29. Potts WJ, Riker WL, DeBord R. An experimental study of respiration maintained by homologous lungs. *J Lab Clin Med*. 1951;38:281–5.
30. Rashkind WJ, Freeman A, Klein D, et al. Evaluation of a disposable plastic, low volume, pumpless oxygenator as a lung substitute. *J Pediatr*. 1965;66:94–102.
31. Meyer A, Strueber M, Fischer S. Advances in extracorporeal ventilation. *Anesthesiol Clin*. 2008;26:381–91.
32. Madershahian N, Wittwer T, Strauch J, et al. Application of ECMO in multitrauma patients with ARDS as rescue therapy. *J Card Surg*. 2007;22:180–4.
33. Perchinsky MJ, Long III WB, Hill JG, et al. Extracorporeal cardiopulmonary life support with heparin-bonded circuitry in the resuscitation of massively injured trauma patients. *Am J Surg*. 1995;169:488–91.
34. Kshettry VR, Kroshus TJ, Hertz MI, et al. Early and late airway complications after lung transplantation: incidence and management. *Ann Thorac Surg*. 1997;63(6):1576–83.
35. Khan NU, Al-Aloul M, Khasati N, et al. Extracorporeal membrane oxygenator as a bridge to successful surgical repair of bronchopleural fistula following bilateral sequential lung transplantation: a case report and review of the literature. *J Cardiothorac Surg*. 2007;2:28.
36. Kirk AJ, Conacher ID, Corri PA, et al. Successful surgical management of bronchial dehiscence after single lung transplantation. *Ann Thorac Surg*. 1990;49(1):147–9.
37. Marasco SF, Lukas G, Mc Donald M, et al. Review of ECMO (extra corporeal membrane oxygenation) support in critically ill adult patient. *Heart Lung Crit*. 2008;17S:S41–7.
38. Kopp R, Dembinski R, Kuhlen R. Role of extracorporeal lung assist in the treatment of acute respiratory failure. *Minerva Anestesiol*. 2006;73:587–95.
39. Segers PAM, Heida JF, De Vries I, et al. Clinical evaluation of nine hollow-fibre membrane oxygenators. *Perfusion*. 2001;16:95–106.
40. Thiara AP, Hoyland V, Norum H, et al. Extracorporeal membrane oxygenation support for 59 days without changing the ECMO circuit: a case of Legionella pneumonia. *Perfusion*. 2009;24(1):45–7.
41. Thiara APS, Hoel TN, Kristiansen F, et al. Evaluation of oxygenators and centrifugal pumps for long-term pediatric extracorporeal membrane oxygenation. *Perfusion*. 2007;22:323–6.
42. Oliver WC. Anticoagulation and coagulation management for ECMO. *Semin Cardiothorac Vasc Anesth*. 2009;13(3):154–74.
43. Beiderlinden M, Treschan T, Goerlinger K, Peters J. Argatroban in extracorporeal membrane oxygenation. *Artif Organs*. 2007;31(6):461–5.
44. Haines NM, Rycus PT, Zwischenberger JB, et al. Extracorporeal life support registry report 2008: neonatal and pediatric cases. *ASAIO J*. 2009;55:111–6.
45. Conrad SA, Rycus PT, Dalton H. Extracorporeal life support registry report 2004. *ASAIO J*. 2005;51:4–10.
46. Plotz FB, van Oeveren W, Bartlett RH, et al. Blood activation during neonatal extracorporeal life support. *J Thorax Cardiovasc Surg*. 1993;105:823–32.
47. Robinson TM, Kickler TS, Walker LK, et al. Effect of extracorporeal membrane oxygenation on platelets in newborns. *Crit Care Med*. 1993;21:1029–34.
48. Stallion A, Cofer B, Rafferty JA, et al. The significant relationship between platelet count and hemorrhagic complications on ECMO. *Perfusion*. 1994;9:265–9.

49. Thelin S, Bagge L, Hultman J, et al. heparin-coated cardiopulmonary bypass circuits reduce blood cell trauma. Experiments in pigs. *Eur J Cardiothorac Surg.* 1991;4:486–91.
50. Videm V, Svennevig JL, Fosse E, et al. Reduced complement activation with heparin-coated oxygenator and tubings in coronary bypass operations. *J Thorac Cardiovasc Surg.* 1992;103:806–12.
51. Borowiec J, Thelin S, Bagge L, et al. Heparin-coated circuits reduce activation of granulocytes during cardiopulmonary bypass. A clinical study. *J Cardiovasc Surg.* 1992;104:806–12.
52. Rastan AJ, Lachmann N, Walther T, et al. Autopsy findings in patients on postcardiotomy extracorporeal membrane oxygenation (ECMO). *Int J Artif Organs.* 2006;29:1121–31.
53. Lidegran MK, Mosskin M, Ringertz HG, et al. Cranial CT for diagnosis of intracranial complications in adult and pediatric patients during ECMO: clinical benefits in diagnosis and treatment. *Acad Radiol.* 2007;14:62–71.
54. Slater JP, Guarino T, Stack J, et al. Cerebral oxygen desaturation predicts cognitive decline and longer hospital stay after cardiac surgery. *Ann Thorac Surg.* 2009;87:36–45.
55. Bulas DI, Taylor GA, O'Donell RM, et al. Intracranial abnormalities in infants treated with extracorporeal membrane oxygenation: update on sonographic and CT findings. *Am J Neuroradiol.* 1996;17:287–94.
56. Vaucher YE, Dudell GG, Bejar R, et al. Predictors of early childhood outcome in candidates for extracorporeal membrane oxygenation. *J Pediatr.* 1996;128:109–17.
57. Stolar CJH, Snedecor SM, Bartlett RH. Extracorporeal membrane oxygenation and neonatal respiratory failure: experience from extracorporeal life support organization. *J Pediatr Surg.* 1991;26:563–71.
58. Risnes I, Wagner K, Nome T, et al. Cerebral outcome in adult patients treated with extracorporeal membrane oxygenation. *Ann Thorac Surg.* 2006;81:1401–7.
59. Jones MD, Hudak ML. Regulation of fetal cerebral circulation. In: Polin RA, Fox WW, editors. *Fetal and neonatal physiology.* Philadelphia: WB Saunders; 1992. p. 682–90.
60. Horton AM, Butt W. Pump-induced hemolysis: is the constrained vortex pump better or worse than the roller pump? *Perfusion.* 1992;7:103–8.
61. Zwischenberger JB, Nguyen TT, Upp JR, et al. Complications of neonatal extracorporeal membrane oxygenation. Collective experience from the extracorporeal life support organization. *J Thorac Cardiovasc Surg.* 1994;107(3):838–48.
62. Paulson OB, Walsemann G, Schmidt JF, et al. Cerebral circulation under normal and pathologic conditions. *Am J Cardiol.* 1989;63(Suppl):2C–5.
63. Graziani LJ, Gringlas M, Baumgart S. Cerebrovascular complications and neurodevelopment sequelae of neonatal ECMO. *Clin Perinatol.* 1997;24:655–75.
64. Holley DG, Short BL, Karr SS, et al. Mechanisms of change in cardiac performance in infants undergoing extracorporeal membrane oxygenation. *Crit Care Med.* 1994;22:1865–70.
65. Bein T, Weber F, Philipp A, et al. A new pumpless extracorporeal interventional lung assist in critical hypoxemia/hypercapnia. *Crit Care Med.* 2006;34(5):1372–7.
66. Brederlau J, Anetseder M, Wagner R, et al. Pumpless extracorporeal lung assist in severe blunt chest trauma. *J Cardiothorac Vasc Anesth.* 2004;18(6):777–9.
67. Fischer S, Hoeper MM, Tomaszek S, et al. Bridge to lung transplantation with the extracorporeal membrane ventilator Novalung in the veno-venous mode: the initial hannover experience. *ASAIO J.* 2007;53(2):168–70.
68. Fischer S, Hoeper MM, Bein T, et al. Interventional lung assist: a new concept of protective ventilation in bridge to lung transplantation. *ASAIO.* 2008;54:3–10.
69. Mattheis G. New technologies for respiratory assist. *Perfusion.* 2003;18(4):245–51.
70. Iglesias M, Martinez E, Badia JR, et al. Extrapulmonary ventilation for unresponsive severe acute respiratory distress syndrome after pulmonary resection. *Ann Thorac Surg.* 2008;85: 237–44.
71. Taylor K, Holtby H. Emergency interventional lung assist device for pulmonary hypertension. *Anesth Analg.* 2009;109:382–5.
72. Kress JP, Pohlmann AS, O'Connor MF. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med.* 2000;342:1471–7.
73. Martin J, Heymann A, Bäsell K, et al. S3 guideline for analgesia, sedation and delirium ICU management. *Ger Med Sci.* 2010;8:Doc 02.
74. Putensen C, Mutz NJ, Putensen-Himmer G, et al. Spontaneous breathing during ventilatory support improves ventilation-perfusion distributions in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1999;159:1241–8.
75. Putensen C, Zech S, Wrigge H, et al. Long-term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. *Am J Respir Crit Care Med.* 2001;164(1):43–9.
76. Deja M, Hommel M, Weber-Carstens S, et al. Evidence-based therapy of severe acute respiratory distress syndrome: an algorithm-guided approach. *JIMR.* 2008;36:211–21.
77. Beiderlinden M, Eikermann M, Boes T, et al. Treatment of severe acute respiratory distress syndrome: role of extracorporeal gas exchange. *Intensive Care Med.* 2006;32(10):1627–31.

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Key Points

- Changes in *right ventricular anatomy and function* can occur at several stages of lung resection, starting after induction of general anesthesia and positioning, followed by one lung ventilation and surgical dissection. Compensatory mechanisms may not occur in patients with advanced COPD who are at risk of developing long-term complications. Several tests are available during the intraoperative period to evaluate right heart function and their merits are reviewed.
- Supraventricular arrhythmias* are a common complication after thoracic surgery, depending on the side and the extent of the dissection. Atrial fibrillation is the most common postoperative rhythm disturbance after lung resection. Several pathophysiologic mechanisms as well as prophylactic and/or therapeutic maneuvers have been proposed. Older age and intrapericardial pneumonectomy are among the risk factors that strongly correlate with this condition.
- Acute coronary syndrome* after thoracic surgery is rare but is associated with a high risk of death. Patients at risk are the ones with preoperative coronary artery disease and abnormal exercise testing. There are no clear recommendations on the role of preoperative cardiac catheterization and coronary revascularization.
- Cardiac failure* can result from either right or left heart dysfunction, and can be transient or long standing. Symptoms may be subtle at rest and become evident during exertion. *Cardiac herniation* is a rare complication that may occur after intrapericardial pneumonectomy and is associated with a high mortality rate. Clinical and electrocardiographic signs are very nonspecific, and treatment is surgical.
- Mediastinal shift* is the result of changes in the postpneumonectomy space. A high index of suspicion is needed for

the diagnosis, which can present with severe hemodynamic compromise or respiratory symptoms. *Postpneumonectomy syndrome* may occur in the late postoperative period. It is characterized by an extreme mediastinal shift which causes dynamic compression of the distal airway and respiratory insufficiency. Treatment is surgical.

Introduction

Lung resection, especially if extensive, can cause acute and chronic changes in right cardiac anatomy and function. This can result from either transient or sustained pressure or volume overload [1], and can be worsened by preexisting abnormalities. Any pathology associated with pulmonary hypertension and chronic hypoxia (such as end stage COPD or connective tissue interstitial lung disease) can cause baseline right ventricular dysfunction (see Table 44.1) [2]. Multiple intraoperative factors, such as induction of general anesthesia, institution of one lung ventilation (OLV) and lateral decubitus, followed by manipulation of the pulmonary circulation or triggering of the inflammatory response, are all known contributors [3]. While cardiac adaptations occur with time after lung resection, cardiac complications, especially arrhythmias, are commonly seen in the immediate postoperative period before patient discharge.

Cardiac Adaptations

Cardiac adaptation can occur in the immediate intraoperative period, after induction of general anesthesia and positioning or in the postoperative phase.

TABLE 44.1. Causes of right ventricular failure.

Pressure overload	Left heart failure (most common) Pulmonary embolus (common) Pulmonary hypertension Right ventricular outflow tract obstruction Peripheral pulmonary stenosis Double chamber right ventricle Systemic right ventricle Tricuspid regurgitation Pulmonary regurgitation Atrial septal defect Anomalous pulmonary venous return Sinus of valsalva rupture in the right atrium Coronary artery fistula in the right atrium or right ventricle Carcinoid syndrome Rheumatic valvulitis Right ventricular myocardial ischemia Cardiomyopathy and heart failure Arrhythmogenic right ventricular dysplasia Sepsis
Volume overload	
Ischemia/infarction	
Intrinsic myocardial processes	
Inflow limitation	Tricuspid stenosis Superior vena cava stenosis
Congenital defects	Ebstein's anomaly Tetralogy of Fallot Transposition of the great vessels Double outlet right ventricle with mitral atresia
Pericardial disease	Constrictive pericarditis

Adapted from Ref. [2]

Intraoperative Changes in Right Ventricular Function and Anatomy Related to One Lung Ventilation and Positioning

Pulmonary arterial pressures can increase after induction of general anesthesia, as a consequence of positive pressure ventilation, placement of the patient in the lateral decubitus, opening of the chest and initiation of OLV [4]. Mediastinal shift, gravity-related changes in pulmonary perfusion and hypoxic vasoconstriction can also contribute to higher pulmonary arterial pressure. In patients with normal pulmonary vascular compliance, an increase in right cardiac output can compensate for the higher afterload without significant changes in pulmonary arterial pressures. This may not occur in patients with advanced COPD, even in the presence of baseline right ventricular hypertrophy [3], theoretically making this population at higher risk for intra- and postoperative cardiac complications. Preexisting significant pulmonary hypertension can worsen during OLV or clamping of the pulmonary artery. Ligation of the main pulmonary artery during pneumonectomy (right more than left), or lung transplantation in patients with severe COPD can cause acute right heart overload and consequent dilation followed by ischemia or arrhythmias, either intra- or postoperatively [5, 6]. A temporary "clamp test" of the pulmonary artery can be done intraoperatively to evaluate the clinical and echocardiographic response of the right heart to acute shifting of blood to the remaining pulmonary circulation. However, this maneuver rarely changes

the intraoperative management, since the results may be difficult to observe or interpret as soon as the clamp is applied. If there are any intraoperative concerns of potential hemodynamic instability or right heart dysfunction, trans-esophageal echocardiography (TEE) can be used by itself or combined with pulmonary arterial catheter data. While TEE is a valuable "real-time" tool to evaluate left ventricular function, its role in assessing right ventricular function is less clear. Despite the superficial location of the right heart, its irregular and asymmetric shape makes the motion and volume calculations much more difficult and less detailed than the left side [1]. In case of high suspicion for perioperative right heart dysfunction, such as in patients with a predicted postoperative FEV₁ less than 40%, detailed preoperative testing becomes extremely important and is highly recommended [7].

Acute and Late Phase Changes in Right Ventricular Anatomy After Lung Resection

Intraoperative increases in resting pulmonary arterial pressure and pulmonary vascular resistance are usually proportional to the extent of the resection, and tend to normalize in the immediate postoperative period. However, right ventricular function slowly declines over time, suggesting adaptive or reactive processes that can lead to right ventricular hypertrophy [4]. The most of the changes in right ventricular ejection fraction are seen during exercise and depend on the level of exertion. Compensatory mechanisms are more efficient during moderate exercise, while at maximal exertion the right ventricular stroke volume becomes fixed at a certain value independently from the increase in the workload and the time from surgery [4]. The extent of the resection and the compensatory volume expansion of the remaining lung can cause changes in the mediastinal anatomy with a rotation of the heart in the chest cavity. Left ventricular function may be affected as well, with changes in filling and contraction. Furthermore, it seems that the degree and efficacy of cardiac compensation after lung resection are significantly better when surgery is performed on younger patients [4].

Lung surgery is currently the most common therapy for non-metastatic resectable lung cancer, as part of a multimodality treatment with chemotherapy [8] and radiation [9]. Nowadays, surgical candidates are much older, due to the improvement in surgical and anesthesia techniques, and with more extensive comorbidities [10], which contribute to a higher risk of postoperative changes in cardiac function. Cardiac and pulmonary diseases are common factors that may significantly influence the postoperative course and increase mortality rates [10]. However, severe pulmonary hypertension (mean pulmonary arterial pressure >45 mmHg) [11] is present only in 3.7% of this patient population, despite their long smoking history and the presence of variable degrees of COPD [12]. Ninety per cent of patients with FEV₁ less than 50% have mean pulmonary arterial pressures of about 20 mmHg, and only 5% may have values greater than 35 mmHg [12].

Several studies have been done to evaluate postoperative right ventricular function (see Table 44.2 [3]). Most of them

TABLE 44.2. Summary of the literature analyzing right ventricular changes after lung surgery.

Study	Time of the study	Type of surgery	Study	Results lobectomy/pneumonectomy	Exclusion	Comments
Venuta et al. [67]	4 years	Lobe (<i>N</i> =26) Pneumonectomy (<i>N</i> =15)	TTE	No changes ↑RVDD ↑PASP moderate TVI	FEV ₁ <60%, h/o MI, angina, valvular ds, AF, cardiac surgery	Mild increase in PASP and RVDD not clinically significant to cause RVH
Foroulis et al. [68]	6 months	Lobe (<i>N</i> =17) Pneumonectomy (<i>N</i> =35)	TTE	↑PASP ↑RVDD ↑TR	Postoperative BPF, empyema, respiratory failure, MI	Small study, higher PASP in pneumonectomy patients at 6 months (R>L cases), with higher incidence of postoperative AF and SVT requiring treatment, attributed to RV dilatation
Amar et al. [24]	1 month	Pneumonectomy (<i>N</i> =70)	TTE	No changes in R and L atrial diameter, EF, TR and RVSP	AF, lung resection, lesser operations, unresectable nonsinus rhythm	Study to evaluate role of diltiazem and digoxin on AF. Echo done as part of their follow up
Amar [60]	1 week	Lobe (<i>N</i> =47) Pneumonectomy (<i>N</i> =39)	TTE	↑HR	↑RSVP ↑HR	RVSP of 31, not affecting RV systolic function unless respiratory failure occurs
Kowalewski et al. [5]	2 days	Lobe (<i>N</i> =9) Pneumonectomy (<i>N</i> =22)	TTE	No changes ↑RVEDV ↓RVEF ↑SVT	Wedge, prior thoracic surgery, nonsinus rhythm	Not very accurate and nonstandard right heart volumes calculations which can underestimate large volumes. RVEF usually underestimates the true value by echo due to RV geometry
Smulders et al. [69]	5 years	Pneumonectomy (<i>N</i> =15)	MRI	R side=cardiac lateral shift. ↓RVEDV, nl LV function L side=rotation, nl RVEDV, ↓LVEF ↑HR, ↓SV	↑HR at 5 years	No signs of RVH at 5 years
Katz et al. [6]	Intraoperative	Lung transplantation (<i>N</i> =32)	TEE	Immediate ↓PAP (systolic+mean), and ↓RV size posttransplantation, normalization of septal geometry in severe pulmonary HTN (↓RVED area)	CPB used in all cases of severe pulmonary HTN	CPB used in all cases of severe pulmonary HTN

All the studies listed are prospective in nature
N number of cases; *TTE* trans-thoracic echocardiography; *PASP* pulmonary arterial systolic pressures; *TVI* tricuspid valve insufficiency; *FEV*, forced expiratory volume at one second; *MI* myocardial infarction; *AF* atrial fibrillation; *RVDD* right ventricular diastolic volume; *RVH* right ventricular hypertrophy; *BPF* bronchopleural fistula; *SVT* supraventricular tachycardia; *RV* right ventricle; *R* right; *L* left; *EF* ejection fraction; *RVEF* right ventricular systolic pressure; *RVEDV* right ventricular end diastolic volume; *RVEF* right ventricular ejection fraction; *MRI* magnetic resonance imaging; *LV* left ventricle; *SV* stroke volume; *TEE* trans-esophageal echocardiography; *PAP* pulmonary arterial pressure; *HTN* hypertension; *CPB* cardiopulmonary bypass

had a small sample size and extremely variable methodology, which makes the results difficult to compare. Some agreement exists for patients after pneumonectomy, where there is an increase in pulmonary arterial systolic pressure and right ventricular diastolic volume or systolic pressure on transthoracic echocardiography [3]. These changes occur in the second post-operative day (POD) and persist after 4 years [3], suggesting an evolution of the cardiovascular response over time [4]. The increase in diastolic volume as well as in pulmonary arterial systolic pressure and the mild tricuspid regurgitation which is observed on two-dimensional echocardiography are all attributed to an increase in both afterload and catecholamine tone after clamping of the pulmonary artery. Despite these changes, 30-day mortality rates seem to be unaffected, except for one study where changes in right ventricular function were associated with respiratory failure and poor FEV₁. Most of the studies showed an increased incidence of tachyarrhythmias after pneumonectomy, which was transient in the majority of cases and not associated with either heart failure or long-term complications [3].

Cardiac Complications

Supraventricular Arrhythmias (Atrial Fibrillation, Atrial Flutter and Supraventricular Tachycardia)

Supraventricular tachyarrhythmias occur in approximately 18% of patients undergoing noncardiac thoracic surgery [13]. The most important risk factors are age of 60 years and older [14] and intrapericardial pneumonectomy [15]. Other markers associated with this complication seem to be an elevated white blood cell (WBC) count on POD one [16] and an elevated perioperative N-terminal-pro-B-type natriuretic peptide [17]. Atrial fibrillation (AF) is the most common rhythm disturbance, followed by supraventricular tachycardia (SVT), atrial flutter and premature ventricular contractions (PVCs). The diagnosis is usually made on the second POD (with a range of 1–7 days), with a good response to pharmacological cardioversion [14, 18–20].

Sustained ventricular tachyarrhythmias are quite rare after lung resection [13]. Nonsustained ventricular tachycardia (more than three consecutive beats) has an incidence of 15% and can occur in the first 96 hours after lung resection, especially in patients with preoperative left bundle branch block [21]. It is rarely associated with hemodynamic instability requiring treatment at any time. There is no association with age, other clinical factors or core temperature upon arrival to PACU. On multivariate analysis, an independent association seems to exist between nonsustained ventricular tachycardia and postoperative atrial fibrillation (POAF). Vagal withdrawal or irritation, and/or a surge in sympathetic activity are all proposed mechanisms. These findings differ from the cardiac surgical literature, where the presence of postoperative ventricular tachycardia often leads to poor outcome [13].

Suggested Risk Factors

POAF can be an isolated complication or associated with respiratory or infectious disease [14]. It is typically transient and reversible and seems to affect individuals with an electrophysiologic substrate for arrhythmias present before or as a result of surgery [22]. Despite the good prognosis, if persistent, POAF is associated with a 1.7% risk of developing cerebrovascular accidents [13]. Thromboembolic events are often responsible and can occur within 24–48 h from the onset of the sustained POAF. If sinus rhythm fails to be restored within this time frame, anticoagulation should be considered weighing the risk of postoperative bleeding [13]. The most recent American Heart Association (AHA) guidelines on management of AF unrelated to surgery provide similar recommendations for which antithrombotic medications one should employ in postoperative patients depending on the patient's risk (i.e., presence of a prosthetic valve, etc., prior cerebrovascular accidents or no risk factors) [23].

Several mechanisms have been proposed to explain POAF, but no consistent factors other than age have been proven. Aging per se has been associated with loss of about 90% of normal sinus nodal fibers [24] and remodeling of the atrial myocardium, with changes in the sinoatrial and atrioventricular nodal conduction, as well as an increased sensitivity to catecholamine activity, especially after surgical trauma in the area [13]. Triggering of the inflammatory response with activation of the complement and several proinflammatory cytokines has also been suggested as a contributing factor for POAF in this age population [25]. This thought is supported by the finding of a doubling in WBCs count that has been observed in patients older than 60 years of age on POD 1, with a threefold increase in the odds of developing POAF [16]. Catecholamine-induced leukocytosis via α and β_2 -receptor activation is a known phenomenon which could in part explain this finding. The use of thoracic epidural analgesia as a modality to cause sympathectomy and prevent POAF has led to disappointing results [26], maybe due to the high individual variability of sympathetic blockade. Other suggested contributing factors include stretching or inflammation of the pulmonary veins, hilar manipulation and mediastinal shift [22]. Aggravating mechanisms are the use of positive inotropic agents, i.e., dopamine, as well as anemia, fever, hypoglycemia, postoperative ischemia and surgical complications [18, 27].

Presenting symptoms of rapid POAF include dyspnea, palpitations, dizziness, syncope, respiratory distress and hypotension. Pulmonary embolism or myocardial ischemia and electrolyte abnormality are most commonly included in the differential diagnosis [28]. According to the AHA guidelines, trans-thoracic echocardiography should be part of the workup for new onset POAF to rule out any structural disease, if such information is not already available [29]. Similarly, the AHA guidelines do not recommend “ruling out” pulmonary embolism, thyrotoxicosis or myocardial ischemia if there are no accompanying clinical signs or symptoms [29].

TABLE 44.3. Proposed risk factors for supraventricular tachyarrhythmias.

Age >60
Male gender
History of paroxysmal atrial fibrillation
Prolonged P wave duration
Preoperative HR >72 bpm
Elevated BNP level
Increased WBC count on POD 1
Intrapericardial procedure

HR heart rate; *bpm* beats per minute; *BNP* brain natriuretic peptide; *WBC* white blood cell count; *POD* postoperative day

Adapted from Refs. [13, 14, 19, 22]

The presence of postoperative arrhythmias is indirectly associated with an increased rate of morbidity. However, in the presence of heart failure or prolonged hypotension, arrhythmias can be a direct cause of death [19]. Length of hospital stay and costs are increased in patients with arrhythmias, highlighting the importance of prevention when possible [14, 30]. In most of the cases, POAF resolves prior to hospital discharge and the great majority of these patients are completely cured at 6 weeks from surgery [25]. Patients are considered at risk for postoperative supraventricular arrhythmias if they have two or more of the risk factors listed in Table 44.3, and if so, they may be started on pharmacological prophylaxis either preoperatively or in the immediate postoperative period. Several regimens are available to prevent or treat atrial tachyarrhythmias.

Role of Medications Used for Treatment or Prevention

β-Blockers have become popular as preventive medications due to their cardioprotective effects. They are used as prophylactic agents with the rationale of counteracting the effects of the high sympathetic tone that occurs after surgery, which may enhance patient susceptibility to dysrhythmias. β-Blockers inhibit intracellular calcium influx via a second messenger and have a membrane stabilizing effect [31]. Their respiratory side effects become particularly important after lung resection since they may worsen pulmonary function in the postoperative period. Pulmonary edema has been described as a potential side effect [32], as well as hypotension and bradycardia. Moreover, in patients on chronic β-blockers, withdrawal may lead to rebound tachycardia and related complications [33]. The β-blocker length of stay study (BLOS) analyzed the effects of β-blockers after cardiac surgery used as prophylactic agents in patients both naïve and already taking β-blockers. The goal was to prevent POAF, and possibly decrease the length of stay in the hospital and ICU. Despite a small decrease in the incidence of POAF in the patients already on a β-blocker, an increased length of stay was observed in the very same group [34]. This was attributed to the development of adverse cardiac and pulmonary effects. Recently, the Perioperative Ischemic Evaluation (POISE) trial showed that aggressive β-blockade in patients at risk or with atherosclerotic disease can reduce

postoperative myocardial infarction and even POAF but at the cost of an increase in mortality related to cerebrovascular events in patients who had hypotension and decreased cerebral perfusion [35]. These findings have been consistent with other trials using lower doses of β-blockers, which questioned the safety of this strategy [36].

Sotalol is a class III antiarrhythmic with significant activity as a nonselective β-blocker and a potassium channel blocker. Potassium current blockade prolongs both the action potential and the QT interval, predisposing to ventricular dysrhythmias such as Torsades de Pointes [33]. This can occur at both therapeutic and toxic dosages [31]. Because of its renal excretion, the use is contraindicated in patients with a creatinine clearance less than 46 mL/min. As with other β-blockers, sotalol is effective in decreasing POAF, but does not reduce hospital length of stay or postoperative morbidity. Bradycardia can be significant enough to stop its use [22]. According to the American College of Cardiology recommendations, sotalol may be harmful if used to pharmacologically cardiovert AF [29]. Unfortunately, most of the data on this medication come from the cardiac surgical population [28].

The *calcium channel blockers* verapamil and diltiazem are used both as prophylactic and therapeutic agents for the treatment of POAF. They decrease intracellular calcium entry by directly blocking the L-type calcium channel and slowing the sino-atrial automaticity and atrio-ventricular nodal conduction [31]. This class of drugs seems to reduce pulmonary vascular resistance and right ventricular pressure as well, making this an attractive option after major lung resection [32]. Hypotension is one of the major side effects, especially with verapamil, and one of the most common reasons to stop these medications. Calcium channel blockers cause a 40% decrease of postoperative myocardial infarction rates and a 45% reduction of ischemia when used in the cardiac surgical population [32]. Diltiazem is superior to digoxin when used to prevent POAF after intrapericardial or standard pneumonectomy [24]. However, both drugs have equal effect on postoperative ventricular ectopy, echocardiographic changes in right ventricular function and hospital length of stay. In the largest study to prevent POAF in thoracic surgical patients, diltiazem was safe and effective in reducing the rate of POAF of almost 50% [30].

Prophylactic *digitalization* to prevent POAF is not recommended any longer since there are no proven benefits and potential associated side effects [37]. Digoxin does not seem to restore normal sinus rhythm in patients with chronic AF, and as a single agent it does not adequately control the ventricular response unless given at very high doses [37], or when combined with β-blockers or calcium channel blockers [38]. Better results are seen when used in patients with chronic AF and heart failure with systolic dysfunction [37]. Digitalis toxicity and the difficulty of assessing proper plasma levels remain the main limiting factors for its use [19]. Moreover, calcium channel blockers have demonstrated to have better results in preventing POAF with fewer side effects [24]. Digoxin should be avoided in patients with renal insufficiency,

electrolyte disturbances (hypokalemia, hypomagnesemia and hypercalcemia), acute coronary syndromes and thyroid disorders. The main mechanism of action is by enhancing vagal stimulation at the atrioventricular node, thus decreasing ventricular response during atrial arrhythmias [33]. There is also an inhibition of the sympathetic response which is unrelated to the increase in cardiac output, and a binding of the myocardial sodium–potassium ATP-ase channel, blocking its transport [38]. The increase in intracellular calcium promotes cardiac contractility.

Amiodarone is a multiple sodium–potassium–calcium channel blocker and a β -adrenergic inhibitor. It is often used to maintain sinus rhythm after electrical cardioversion in the general population. As a prophylactic agent, it works best when administered 1 week prior to cardiac surgery [39]; however, the precise mechanism of action is unknown [40]. The sodium–calcium–potassium channel blockade causes an increase in the duration of the action potential and the refractory period in the cardiac tissue. As a result, hypotension, bradycardia and QT prolongation can be significant, especially in patients with congestive heart failure and left ventricular dysfunction [27]. Other side effects seen with prolonged use include hypo or hyperthyroidism, hepatic and neurotoxicity, and prolongation of warfarin half-life [40]. However, pulmonary toxicity remains the main concern of amiodarone therapy after lung resection [32]. It can occur at lower dosages than the ones used in the general population, and can manifest as chronic interstitial pneumonitis, bronchiolitis obliterans, adult respiratory distress syndrome (ARDS) or a solitary lung mass [27]. In a very small prospective randomized study, Van Mieghem et al. [41] examined the role of amiodarone prophylaxis on POAF after lung resection, and compared it to verapamil. The interim analysis showed no difference between the two drugs. However, the study was stopped prematurely due to an increased incidence of ARDS in the amiodarone group (7.4% in the patients who had a right pneumonectomy vs. 1.6% for other types of lung resections), and a higher mortality rate. This occurred despite using standard intravenous regimens and having therapeutic plasma concentrations. Two mechanisms were proposed: an indirect one, by increasing inflammatory mediators, and a direct one, by causing direct damage to the cells and subsequent fibrosis. Independently from the etiology, they recommended to avoid amiodarone after lung resection. By surgically decreasing the amount of lung parenchyma available, standard doses of amiodarone can account for higher pulmonary concentrations of the drug which may reach toxic levels. These results were not confirmed by later studies, when amiodarone was used for a short time period [13]. A recent prospective randomized study on 130 patients undergoing to lung resection showed a decreased incidence of AF in the amiodarone group (13.8 vs. 32.3% in the control), with no difference in respiratory or cardiac complications [42]. The lack of double blinding and the selection bias represented by a high exclusion rate of cases of intraoperative AF are the main limitations for this study. Overall, the efficacy of

amiodarone in preventing POAF does not seem to be different from diltiazem [13]. Its main indication still remains as a second tier drug for POAF refractory to rate control drugs or as a therapeutic agent for POAF coupled with preexcitation conduction abnormalities, such as Wolff–Parkinson–White syndrome [29].

Magnesium is indicated in the case of hypomagnesemia. The data on the use of magnesium are mainly from the cardiac surgical literature and are conflicting. One randomized controlled study done on 200 patients undergoing cardiopulmonary bypass surgery showed a decreased incidence of POAF when magnesium sulfate was administered for prophylaxis [43]. However, several other trials in similar surgical population have given conflicting results on the benefits of magnesium and POAF prophylaxis, with the only agreement to maintain magnesium levels within normal values [33]. Except in patients with acute renal failure, magnesium has a relatively safe profile.

Statins (3-hydroxy-3-methylglutararyl coenzyme-A reductase inhibitors) have been shown to suppress electrical remodeling and prevent POAF in animal models [27]. They are powerful lipid lowering drugs highly effective in preventing coronary artery disease [23]. Studies conducted in hypercholesterolemic patients on statins undergoing coronary artery bypass grafting (CABG) showed a decrease in postoperative major cardiac events [44]. This effect was potentiated by simultaneously taking β -blockers [45]. The main benefits of statins seem to occur when these drugs are started in the preoperative period. When administered one week prior to on pump CABG, they decreased the incidence of POAF, as well as hospital length stay [22, 45]. After major lung resection, patients already on statins prior to surgery showed a threefold decrease in the probability of developing POAF [46]. One possible explanation seems to be related to their antiinflammatory or antioxidant mechanism, and observational studies conducted in patients undergoing major lung resection have observed an increase in C-reactive protein and interleukin 6 in the postoperative period [47].

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have been suggested to reduce the incidence of POAF in patients with coexisting heart failure and systolic left ventricular dysfunction, but not in cases associated with systemic hypertension [48]. They may also play a role in maintaining sinus rhythm after electrical cardioversion. The data in the literature have focused mainly on the role of these drugs on the outcome in patients with chronic AF. The prophylactic use of ACEIs/ARBs to prevent POAF remains quite controversial, with both positive [22] and negative [49] findings. Inhibition of the renin–angiotensin–aldosterone system seems to attenuate left atrial dilatation, atrial fibrosis and to contribute in slowing conduction in animal studies, all factors that can trigger and maintain reentry circuits. These effects seem to be potentiated in patients with chronic heart failure when β -blockers are added [22].

Role of Postoperative Chemical and Electrical Cardioversion

Chemical and electrical cardioversion: Pharmacological cardioversion seems to be the most effective when started within 7 days from the onset of AF [29]. Drugs that can chemically cardiovert AF with variable success include flecainide, propafenone and ibutilide [13]. Ibutilide has been shown to have modest success in converting acute AF after cardiac surgery, and it may be associated with polymorphic ventricular tachycardia, especially in the presence of electrolyte abnormality [29]. Single oral doses of flecainide (300 mg) or propafenone (600 mg) seem to be safe, cardioverting, respectively, 91 and 76% of the cases within 8 hours from the onset of AF. In order to be eligible to receive these drugs, patients must be free from cardiac structural disease, such as left ventricular hypertrophy, mitral valve disease, coronary artery disease or heart failure [50]. The potential side effects for both drugs include ventricular tachycardia, heart failure and conversion to atrial flutter with rapid ventricular response [29].

Electrical cardioversion is used to treat AF in case of hemodynamic instability, with a success rate of 67–94% [27]. Biphasic waveforms are more successful than monophasic, using a current around 100–200 J and in a synchronized mode. Higher energy can be used for patients with high body mass index, prolonged AF or left atrial enlargement. Bradycardia (more common in patients on antiarrhythmics prior to cardioversion), ventricular tachyarrhythmias (in case of shock applied during repolarization), hypotension, pulmonary edema (probably due to myocardial stunning) and embolism are all potential complications. Electrolytes should be checked and normalized before cardioversion. In the case of digitalis toxicity and hypokalemia, cardioversion should be avoided due to the high incidence of ventricular fibrillation. In this setting, low currents and prophylactic lidocaine should be used. Since bradycardia can be profound up to the point of asystole, pacing capabilities should be also readily available [27].

Acute Coronary Syndrome

Myocardial ischemia may occur transiently after lung resection and be present as an electrocardiographic finding in 3.8% of patients, while infarction can occur in 0.2–0.9% of the cases [8, 51, 52]. The diagnosis of symptomatic perioperative myocardial infarct is associated with a 30–50% risk of death [23]. The incidence is increased in the presence of preoperative coronary artery disease and abnormal exercise testing. Patients are at the highest risk during the first three PODs, when a high degree of monitoring is suggested.

There are no definite recommendations for preoperative invasive testing or interventions. Most of the decision making should be based on the clinical presentation [53]. In patients at high risk (such as the ones with unstable angina, uncompensated chronic heart failure, arrhythmias and severe valvular disease) cardiac catheterization is highly recommended and

followed by coronary artery revascularization, if necessary [28]. There are no prospective randomized studies on prophylactic CABG prior to elective surgery and whether this is superior to percutaneous revascularization (PCI). If patients require revascularization, elective surgery needs to be postponed, with the dilemma of how long to wait, especially in the case of cancer, where there is potential disease progression [54]. Cardiac stents, especially the drug eluting ones, represent a significant problem due to the prolonged need for anticoagulation. Stopping dual antiplatelet therapy (aspirin and clopidogrel) is associated with a quite high risk of stent thrombosis, while continuing it leads to an increased risk of intra- and postoperative bleeding and precludes the possibility of using regional anesthetic techniques [55]. The duration of the anticoagulation is usually based upon the type of stent: 4–6 weeks for bare metal stents and 12–24 months for drug eluting ones [23]. The risk of stent thrombosis is higher for drug eluting stents, especially if the stent is long, at a bifurcation, if the revascularization is incomplete, or the patient has history of diabetes or heart failure [56]. A nonrandomized observational prospective study done in noncardiac surgery patients who had cardiac stents placed within a year from surgery found a 44.7% rate of postoperative cardiac complications and a 4.7% mortality rate [57]. The dual antiplatelet therapy was stopped on average 3 days prior to surgery and substituted with intravenous unfractionated heparin or subcutaneous enoxaparin. Most of the complications occurred within the first 35 days from the stent placement and were cardiac in nature. Bleeding was not a significant variable. Despite the absence of randomization and the lack of information about the type of stent used, this study stresses several important points. Once the antiplatelet treatment is stopped, low molecular weight heparin should be used (heparin alone is insufficient); all non life saving procedures should be postponed at least for 6–12 weeks from the stent placement, and aspirin should be continued as long as possible prior to surgery [55, 57]. Prophylactic revascularization (CABG vs. PCI) does not seem to add further benefits over optimal medical treatment in patients with cardiac risk undergoing elective major vascular surgery [54]. Long-term survival as well as myocardial infarction, death and hospital length of stay seems to be unchanged. However, CABG is associated with less postoperative myocardial infarctions and decreased hospital length of stay when compared to PCI, probably because of better revascularization [58]. According to the American College of Cardiology, revascularization should be reserved for patients with unstable angina or advanced coronary artery disease [23]. In case the stents need to be placed before surgery, bare metal stents are preferred due to their lower risk of thrombosis. In both cases, elective surgery needs to be appropriately delayed to prevent graft or stent thrombosis.

Heart Failure and Cardiac Herniation

Heart failure can occur after major lung resection as a result of right or left sided dysfunction. *Right heart failure* can result

from changes either in contractility or afterload. Unfortunately, most of the studies looking at changes in right ventricular function after lung resection were small, and found minor and transient differences when compared to the preoperative period. An increase in right ventricular end-diastolic volume has been observed as a reversible finding during the first two PODs [28], as well as a mild increase in pulmonary arterial pressures and pulmonary vascular resistance [59]. While postoperative changes in pulmonary arterial pressures, central venous pressures and pulmonary vascular resistance seem to be subtle at rest, they may become significant during exercise. Changes in right ventricular function are usually able to compensate for the former, but they may fail for the latter, leading to pulmonary hypertension [28]. When trans-thoracic echocardiography has been used to evaluate right ventricular function after pneumonectomy, it has shown only a mild increase in pulmonary arterial pressure which is not associated with ventricular dysfunction [60]. Other possible causes of right ventricular failure, although rare, include pulmonary embolism and cardiac herniation. *Left side heart failure* is usually a consequence of right heart dysfunction, either by decreasing left ventricular preload or shifting the interventricular septum [28]. Acute ischemia and valvular disease may also be contributing factors. *Cardiac herniation*, a rare complication after pneumonectomy, may be responsible for both right and left heart failure. It occurs more commonly after intrapericardial pneumonectomy, right more than left, and leads to a 50% mortality rate [28]. Herniation can be secondary to an incomplete surgical closure of the pericardium or the breakdown of a pericardial patch [61]. One main contributing factor includes an increase in intrathoracic pressure, such as with coughing. Changes in position, with the operative side being dependent, positive pressure ventilation, rapid lung reexpansion or suction on the chest tube are all other possible causes. Symptoms depend on the side of the herniation. Right-sided cases present with superior vena cava syndrome, due to kinking of the superior vena cava and decreased right ventricular filling, with subsequent hypotension, tachycardia and shock. Left-sided cases present with arrhythmias and ischemia, causing myocardial infarction, hypotension and ventricular fibrillation if left untreated [62]. This appears to be related to less cardiac rotation, with subsequent pericardial compression on the myocardium. Clinical presentation and electrocardiographic findings are fairly nonspecific in suggesting the diagnosis, stressing the role of chest radiography and a high index of suspicion. Treatment is surgical, with repositioning of the heart and placement of a patch. In order to minimize hemodynamic instability, the patient should be kept on the lateral decubitus with the operative side up [61].

Mediastinal Shift and Postpneumonectomy Syndrome

Mediastinal shift can occur intraoperatively or in the postoperative period as a result of changes in the postpneumonectomy space. At the end of surgery, once the chest is closed, some surgeons evacuate the air and fluid that fills the empty

space aiming to bring the mediastinum back to midline. Excessive fluid drainage can lead to ipsilateral mediastinal shift and contralateral lung expansion, with decreased venous return and significant hypotension [63]. A high index of clinical suspicion, careful monitoring of the hemodynamics and communication with the surgical team are needed at this point of the operation to avoid hemodynamic collapse. When excessive fluid accumulates in this space, contralateral mediastinal shift occurs, leading to compression of the remaining lung and secondary respiratory insufficiency. This is seen more often in the postoperative period, and the use of intracavitory pressures monitoring can guide the drainage of the excess fluid if needed [63]. CT scan studies have shown obliteration of the postpneumonectomy space with fluid over time, elevation of the hemidiaphragm and expansion of the contralateral lung [64]. In the case of extreme mediastinal shift, dynamic compression of the distal airway can occur, leading to the so-called “*postpneumonectomy syndrome*” [65, 66]. This is a rare and late complication, which can occur at a median of 7 years from surgery. It is more common in females, children and with right-sided procedures (even though it has been described for left cases as well). It manifests with exertional respiratory insufficiency, stridor and recurrent infections. Respiratory symptoms are caused by dynamic compression of the distal trachea and mainstem bronchus and treatment involves the use of airway stents or thoracotomy and repositioning of the mediastinum via saline filled prosthesis (see also Chap. 41).

Conclusion

In the last few decades, a significant improvement in the surgical and anesthetic techniques has made pneumonectomy and major lung resection safer. The introduction of epidural analgesia, minimally invasive surgical techniques and the introduction of short acting anesthetics have all contributed to decrease the incidence of postoperative complications. Fast track strategies and careful selection of patients undergoing to lung resection procedures have also played an important role in postoperative and long-term outcome. Better utilization of step down and acute postoperative care units have decreased the rate of ICU admissions, saving costs. Since the average age of patients requiring lung resection is increasing, anesthesiologists and surgeons will be facing more complex cases, due to the presence of multiple comorbidities. Careful preoperative work up, customizing the type of surgery as well as planning for in hospital and post discharge rehabilitation options will prove to be essential for decreasing even further the possible complications and improving the overall care.

Clinical Case Discussion

A 65-year-old-man with squamous cell cancer of the right upper lobe underwent a right intrapericardial pneumonectomy. Surgery was 150 min and uneventful. Estimated blood



FIG. 44.1. Radiographic changes on postoperative days 2.

loss was 700 cc, and 700 cc of ringer's lactate was used during the case. Urinary output was 100 cc. The patient was extubated in the operating room at the end of the case. A thoracic epidural was used intraoperatively, and the patient was comfortable in PACU. As part of the postoperative blood work, troponin levels were checked and the first set was 1.66 (1.07 and 0.52 the second and the third one). ST segment elevations transiently occurred on POD 1 in correspondence to a fourth troponin of 1.55.

On POD 2, subcutaneous emphysema was noted on the right chest wall, neck and eye (see Fig. 44.1). While walking, he had an episode of desaturation and tachycardia. Chest X-ray is shown. Electrocardiogram showed rapid SVT, with hypotension (HR=128, BP=88/45). The patient was transferred to the ICU where he was intubated. He slowly became hemodynamically unstable, requiring multiple pressors.

CXR on POD 2

Questions

What are common cardiac complications after lung resection?

- Arrhythmias (atrial fibrillation, atrial flutter and SVT).
- Ischemia and acute coronary syndrome.
- Heart failure and cardiac herniation.
- Mediastinal shift and postpneumonectomy syndrome.

Specifically:

- Arrhythmias: Who is at risk (suggested pathophysiology, role of WBC and inflammatory response, BNP levels)? What we can do to prevent it (rate or rhythm control? Pre-operative medications?)? How do we treat postoperatively (medications vs. cardioversion)? Risks/side effects of the treatment.

- Acute coronary syndrome: What are known risk factors? Preoperative stenting vs. medical treatment for patients with a positive stress test. Is myocardial ischemia preventable (role of preoperative statins/beta blockers)? What is the treatment? How does it affect mortality?
- Cardiomegaly/cardiac failure: Who is at risk (role of the extent of dissection, preoperative risk factors)? How does it affect mortality?
- Mediastinal shift: Why does this happen (extent of dissection)? How common is cardiac herniation? Pathophysiology and diagnosis.

References

1. Ho SY, Nihoyannopoulos P. Anatomy, echocardiography, and normal right ventricular dimensions. *Heart*. 2006;92 Suppl 1: i2–13.
2. Haddad F et al. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. *Circulation*. 2008;117(13):1717–31.
3. Pedoto A, Amar D. Right heart function in thoracic surgery: role of echocardiography. *Curr Opin Anaesthesiol*. 2009;22(1):44–9.
4. Heerdt PM, Malhotra J, editors. The right ventricular response to lung resection. *Progress in Thoracic Anesthesiology*. 2004. p. 221–46.
5. Kowalewski J et al. Right ventricular morphology and function after pulmonary resection. *Eur J Cardiothorac Surg*. 1999;15(4): 444–8.
6. Katz WE et al. Immediate effects of lung transplantation on right ventricular morphology and function in patients with variable degrees of pulmonary hypertension. *J Am Coll Cardiol*. 1996;27(2):384–91.
7. Slinger PD, Johnston MR. Preoperative assessment: an anesthesiologist's perspective. *Thorac Surg Clin*. 2005;15(1):11–25.
8. Martin J et al. Morbidity and mortality after neoadjuvant therapy for lung cancer: the risks of right pneumonectomy. *Ann Thorac Surg*. 2001;72(4):1149–54.
9. Van Schil PE. Surgery: therapeutic indications. *Cancer Radiother*. 2007;11(1–2):47–52.
10. Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care unit versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22(1):50–5.
11. McLaughlin VV et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573–619.
12. Falk JA et al. Cardiac disease in chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2008;5(4):543–8.
13. Amar D. Prevention and management of perioperative arrhythmias in the thoracic surgical population. *Anesthesiol Clin*. 2008;26(2):325–35; vii.
14. Roselli EE et al. Atrial fibrillation complicating lung cancer resection. *J Thorac Cardiovasc Surg*. 2005;130(2):438–44.
15. Dancewicz M, Kowalewski J, Peplinski J. Factors associated with perioperative complications after pneumonectomy for primary carcinoma of the lung. *Interact Cardiovasc Thorac Surg*. 2006;5(2):97–100.

16. Amar D et al. Leukocytosis and increased risk of atrial fibrillation after general thoracic surgery. *Ann Thorac Surg*. 2006;82(3):1057–61.
17. Cardinale D et al. Increased perioperative N-terminal pro-B-type natriuretic peptide levels predict atrial fibrillation after thoracic surgery for lung cancer. *Circulation*. 2007;115(11):1339–44.
18. Vaporciyan AA et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. *J Thorac Cardiovasc Surg*. 2004;127(3):779–86.
19. Foroulis CN et al. Factors associated with cardiac rhythm disturbances in the early post-pneumonectomy period: a study on 259 pneumonectomies. *Eur J Cardiothorac Surg*. 2003;23(3):384–9.
20. Bobbio A et al. Postoperative outcome of patients undergoing lung resection presenting with new-onset atrial fibrillation managed by amiodarone or diltiazem. *Eur J Cardiothorac Surg*. 2007;31(1):70–4.
21. Amar D, Zhang H, Roistacher N. The incidence and outcome of ventricular arrhythmias after noncardiac thoracic surgery. *Anesth Analg*. 2002;95(3):537–43; table of contents.
22. Mayson SE et al. The changing face of postoperative atrial fibrillation prevention: a review of current medical therapy. *Cardiol Rev*. 2007;15(5):231–41.
23. Fleisher LA et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol*. 2009;54(22):e13–118.
24. Amar D, et al. Effects of diltiazem versus digoxin on dysrhythmias and cardiac function after pneumonectomy. *Ann Thorac Surg*. 1997;63(5):1374–81; discussion 1381–2.
25. Amar D. Post-thoracotomy atrial fibrillation. *Curr Opin Anesthesiol*. 2007;20(1):43.
26. Ahn HJ et al. Thoracic epidural anesthesia does not improve the incidence of arrhythmias after transthoracic esophagectomy. *Eur J Cardiothorac Surg*. 2005;28(1):19–21.
27. Crawford TC, Oral H. Cardiac arrhythmias: management of atrial fibrillation in the critically ill patient. *Crit Care Clin*. 2007; 23(4):855–72; vii.
28. Karamichalis JM, Putnam Jr JB, Lambright ES. Cardiovascular complications after lung surgery. *Thorac Surg Clin*. 2006;16(3): 253–60.
29. Fuster V et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114(7):e257–354.
30. Amar D et al. Effects of diltiazem prophylaxis on the incidence and clinical outcome of atrial arrhythmias after thoracic surgery. *J Thorac Cardiovasc Surg*. 2000;120(4):790–8.
31. DeWitt CR, Waksman JC. Pharmacology, pathophysiology and management of calcium channel blocker and beta-blocker toxicity. *Toxicol Rev*. 2004;23(4):223–38.
32. Sedrakyan A et al. Pharmacologic prophylaxis for postoperative atrial tachyarrhythmia in general thoracic surgery: evidence from randomized clinical trials. *J Thorac Cardiovasc Surg*. 2005; 129(5):997–1005.
33. Bradley D et al. Pharmacologic prophylaxis: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005;128(2 Suppl):39S–47.
34. Connolly SJ et al. Double-blind, placebo-controlled, randomized trial of prophylactic metoprolol for reduction of hospital length of stay after heart surgery: the beta-Blocker Length Of Stay (BLOS) study. *Am Heart J*. 2003;145(2):226–32.
35. Devereaux PJ et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371(9627):1839–47.
36. Fleisher LA, Poldermans D. Perioperative beta blockade: where do we go from here? *Lancet*. 2008;371(9627):1813–4.
37. Tamargo J, Delpon E, Caballero R. The safety of digoxin as a pharmacological treatment of atrial fibrillation. *Expert Opin Drug Saf*. 2006;5(3):453–67.
38. Gheorghiade M, Adams Jr KF, Colucci WS. Digoxin in the management of cardiovascular disorders. *Circulation*. 2004;109(24): 2959–64.
39. Mitchell LB et al. Prophylactic oral amiodarone for the prevention of arrhythmias that begin early after revascularization, valve replacement, or repair: PAPABEAR: a randomized controlled trial. *JAMA*. 2005;294(24):3093–100.
40. Zimetbaum P. Amiodarone for atrial fibrillation. *N Engl J Med*. 2007;356(9):935–41.
41. Van Mieghem W et al. Amiodarone and the development of ARDS after lung surgery. *Chest*. 1994;105(6):1642–5.
42. Tisdale JE, et al. A randomized trial evaluating amiodarone for prevention of atrial fibrillation after pulmonary resection. *Ann Thorac Surg*. 2009;88(3):886–93; discussion 894–5.
43. Toraman F, et al. Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg*. 2001;72(4):1256–61; discussion 1261–2.
44. Thielmann M et al. Lipid-lowering effect of preoperative statin therapy on postoperative major adverse cardiac events after coronary artery bypass surgery. *J Thorac Cardiovasc Surg*. 2007; 134(5):1143–9.
45. Patti G et al. Randomized trial of atorvastatin for reduction of postoperative atrial fibrillation in patients undergoing cardiac surgery: results of the ARMYDA-3 (atorvastatin for reduction of myocardial dysrhythmia after cardiac surgery) study. *Circulation*. 2006;114(14):1455–61.
46. Amar D et al. Statin use is associated with a reduction in atrial fibrillation after noncardiac thoracic surgery independent of C-reactive protein. *Chest*. 2005;128(5):3421–7.
47. Amar D et al. Inflammation and outcome after general thoracic surgery. *Eur J Cardiothorac Surg*. 2007;32(3):431–4.
48. Healey JS et al. Prevention of atrial fibrillation with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: a meta-analysis. *J Am Coll Cardiol*. 2005;45(11):1832–9.
49. Coleman CI et al. Effect of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers on the frequency of post-cardiothoracic surgery atrial fibrillation. *Ann Pharmacother*. 2007;41(3):433–7.
50. Amar D. Postthoracotomy atrial fibrillation. *Curr Opin Anesthesiol*. 2007;20(1):43–7.
51. Boffa DJ et al. Data from The Society of Thoracic Surgeons General Thoracic Surgery database: the surgical management of primary lung tumors. *J Thorac Cardiovasc Surg*. 2008;135(2):247–54.
52. Allen MS, et al. Morbidity and mortality of major pulmonary resections in patients with early-stage lung cancer: initial results of the randomized, prospective ACOSOG Z0030 trial. *Ann Thorac Surg*. 2006;81(3):1013–9; discussion 1019–20.

53. Jaroszewski DE et al. Utility of detailed preoperative cardiac testing and incidence of post-thoracotomy myocardial infarction. *J Thorac Cardiovasc Surg.* 2008;135(3):648–55.
54. McFalls EO et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med.* 2004;351(27):2795–804.
55. Spahn DR et al. Coronary stents and perioperative anti-platelet regimen: dilemma of bleeding and stent thrombosis. *Br J Anaesth.* 2006;96(6):675–7.
56. Albaladejo P et al. Perioperative management of antiplatelet agents in patients with coronary stents: recommendations of a French Task Force. *Br J Anaesth.* 2006;97(4):580–2.
57. Vicenzi MN et al. Coronary artery stenting and non-cardiac surgery – a prospective outcome study. *Br J Anaesth.* 2006;96(6):686–93.
58. Ward HB, et al. Coronary artery bypass grafting is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery. *Ann Thorac Surg.* 2006;82(3):795–800; discussion 800–1.
59. Reed CE, Spinale FG, Crawford Jr FA. Effect of pulmonary resection on right ventricular function. *Ann Thorac Surg.* 1992;53(4):578–82.
60. Amar D et al. Value of perioperative Doppler echocardiography in patients undergoing major lung resection. *Ann Thorac Surg.* 1996;61(2):516–20.
61. Slinger P. Update on anesthetic management for pneumonectomy. *Curr Opin Anaesthesiol.* 2009;22(1):31–7.
62. Mehanna MJ et al. Cardiac herniation after right pneumonectomy: case report and review of the literature. *J Thorac Imaging.* 2007;22(3):280–2.
63. Wolf AS, et al. Managing the pneumonectomy space after extrapleural pneumonectomy: postoperative intrathoracic pressure monitoring. *Eur J Cardiothorac Surg.* 2010.
64. Biondetti PR et al. Evaluation of post-pneumonectomy space by computed tomography. *J Comput Assist Tomogr.* 1982;6(2):238–42.
65. Bedard EL, Uy K, Keshavjee S. Postpneumonectomy syndrome: a spectrum of clinical presentations. *Ann Thorac Surg.* 2007;83(3):1185–8.
66. Shen KR, et al. Postpneumonectomy syndrome: surgical management and long-term results. *J Thorac Cardiovasc Surg.* 2008;135(6):1210–6; discussion 1216–9.
67. Venuta F et al. Long-term Doppler echocardiographic evaluation of the right heart after major lung resections. *Eur J Cardiothorac Surg.* 2007;32(5):787–90.
68. Foroulis CN et al. Study on the late effect of pneumonectomy on right heart pressures using Doppler echocardiography. *Eur J Cardiothorac Surg.* 2004;26(3):508–14.
69. Smulders SA et al. Cardiac function and position more than 5 years after pneumonectomy. *Ann Thorac Surg.* 2007;83(6):1986–92.

45

Postthoracotomy Surgical Management and Complications

Dirk Wagnetz and Marc de Perrot

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Key Points

- Chest drains can usually be removed postthoracotomy when the air leak has stopped and drainage is <300 mL/day.
- The majority of thoracic surgical patients are at high risk for postoperative venous thromboembolism.
- Postthoracotomy blood loss via the chest drains requires reexploration if it meets or exceeds 1 L in 1 h or 200 mL/h for 4 h.
- The risk of postthoracotomy hemorrhage is increased in patients with a previous thoracotomy and following decortication or surgery for infectious causes.
- Lobar torsion most often occurs in the right middle lobe following a right upper lobectomy.

General Principles of Postoperative Care

In thoracic surgery, perhaps more than in any other surgical field, “an ounce of prevention is worth a pound of cure.” To obtain best results in perioperative care after pulmonary procedures this care begins before the procedure and does not end until long after the patient leaves the hospital.

Preoperative Preparation

Preoperative Teaching

To achieve the best participation in a patient’s postoperative care, the patient and family should be as fully informed as possible. When both patient and family know what to expect, they are better prepared to deal with the problems as they arise.

The surgeon should have frank and open discussions with the patient and family concerning the anticipated outcome and expected postoperative problems, along with the usual measures to combat those problems. Such discussions help the patient and family understand that the postoperative course may not be smooth and that aggressive measures may be required to achieve ultimate recovery. According to Wright et al., the most common problems delaying discharge from the hospital include inadequate pain control, prolonged air leak, severe nausea, fever, debility, and arrhythmias [1] (Table 45.1).

Preoperative Pulmonary Exercise and Training

The role of pulmonary rehabilitation is more controversial. In 1979, Gracey et al. [2] studied 157 patients who were about to undergo a major operation. They administered a standard pulmonary preparation program used at that time and found that complications were significantly reduced but also that postoperative pulmonary complications were related to the extent of the operation. In 1999, Debigare et al. [3] studied preparation for lung volume reduction procedures for severe emphysema. Because many patients traveled a great distance, the investigators devised a home exercise training program that included incentive spirometry, muscle exercises, and aerobic training. It began with detailed teaching and follow-up and was ensured through weekly phone calls and a diary filled out by each patient. As a result, there was a significant increase in the 6-minute walk test, quality-of-life perception, peak work rate, peak oxygen consumption, endurance time, and muscle strength; it was therefore concluded that such training was beneficial when time permits a delay in the timing of the operation. This time delay may however not always be an option in patients with malignancy.

Smoking

Smoking cessation has always been considered an important issue in preparation for an operation. However, the evidence shows that the effects of cigarette smoking linger long after cessation and that inordinately long preoperative delays would be necessary to achieve any significant improvement. The Lung Health Study Research Group has published many reports concerning the effects of smoking cessation. Anthonisen et al. [4] reported the results of one of the aforementioned group's studies involving individuals with documented early chronic obstructive pulmonary disease (COPD) who stopped smoking; they experienced improvement of lung function, with the greatest benefit being noted in the first year. No conclusions can be drawn concerning the early effects of smoking cessation, because the investigators first observation point was 3 months after intervention. Despite the lack of firm evidence, it is still recommended that patients quit smoking for as long as possible prior to operation. Some data suggest that cessation of smoking could potentially lead to higher postoperative complications. This is based on the fact that patients have increased secretions early after cessation [5]. However, in 2005, Barrera [6] studied smokers undergoing thoracotomy at Memorial Sloan-Kettering Cancer Center. They found no difference in pulmonary complications among recent quitters vs. continuing smokers. Only patients with >60 packs per year and those with a significantly reduced diffusion capacity had

a higher risk for postoperative pneumonia in that series. The investigators concluded that it was safe to quit at any time before operation.

Medication

Preoperative medications should be continued up to the time of operation. The only exceptions are anticoagulant medications. Patients on warfarin (Coumadin), therapeutic doses of low-molecular-weight heparin, or clopidogrel (Plavix) should stop their medications long enough prior to the procedure. It is our practice to recommend patients to stay on aspirin at the time of their surgery to decrease the risk of postoperative cardiac complications. The use of aspirin has not been associated with increased risk of bleeding in our experience. There is also no evidence that the addition of preoperative short-term bronchodilators changes operative outcomes.

Postoperative Management

Chest Drainage System

Surgeons have several different options for draining the chest. Most surgeons still place two #28 Fr chest tubes, one anteriorly and one posteriorly in the chest. The tubes are attached to a drainage system that permits one-way drainage only, with a portion of the device set up to collect fluid (Fig. 45.1). These devices use a variety of valves or liquid to establish a one-way system. All of the collection systems are designed to provide suction on the tubes if the surgeon desires. In the past, all chest tubes were placed on suction at $-20\text{ cm H}_2\text{O}$. In recent years, the advisability of the ubiquitous use of suction has been questioned. Several investigators, like Cerfolio, and Wain and their respective coworkers, contend that if the lung is fully expanded with the tube on no suction, the patient will do well. Hence there is currently more individual preference concerning chest tube suction. In our institution suction at $-20\text{ cm H}_2\text{O}$ is preferred at least for 24 h and a chest

TABLE 45.1. Common reasons for delay in discharge.

Cause	Percentage
Inadequate pain control	28
Prolonged air leak	19
Severe nausea	17
Fever	16
Debility	12
Atrial arrhythmia	7

Adapted from Wright et al. [1]

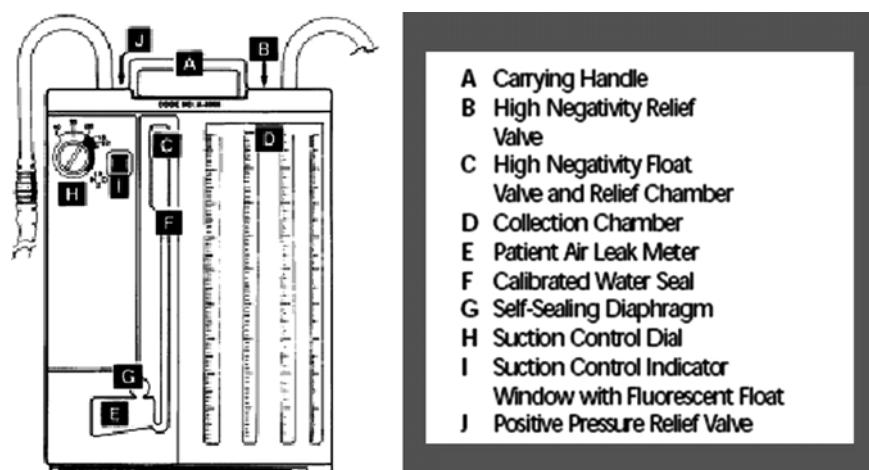


FIG. 45.1. Chest tube drainage system with high- and low-pressure relief valves.

X-ray showing a fully expanded lung the next day. Exceptions are patients with significant emphysema or pneumonectomy or after volume reduction surgery. When pleural apposition is not realistically achievable, suction can potentially prolong the air leak in these patients.

A special consideration with respect to chest drainage is after pneumonectomy. Traditional water seal devices allow egress of air out from the pleural cavity but not for its return. This can lead to progressive mediastinal shift after pneumonectomy. There are several possible solutions. A chest drain need not be left at all, if the risk of bleeding is minimal. The mediastinum can be balanced by removing a few hundred milliliters of air as the thoracotomy is being closed, by means of a red rubber catheter. In addition, a needle thoracocentesis can be performed in the recovery room after the postoperative chest radiograph is reviewed. If bleeding is sufficient to require drainage, a balanced pneumonectomy chest drainage system is available. This device allows air both in and out, to keep the pleural space within a preset range. Alternatively, a traditional system may be used but clamped and only intermittently opened, although this approach is vulnerable to missteps by inexperienced staff.

Regardless of types of chest tubes and the use of suction, the drainage tubes must be assessed at least daily for patency, function, air leakage, and drainage. Inspection of the tube and drainage system for clots or blockages assures patency. Obstructions are removed by "milking" or "stripping" the tubing. This is accomplished by occluding the tubing and pulling it away from the patient to produce a local suction effect. If this does not work, a balloon-tipped catheter may be passed up the tubing to remove the clot, or a suction catheter may be used for the same purpose. A functioning tube is the one that shows variation in the fluid within it when the patient breathes quietly. This may be observed while talking with the patient at the bedside. Good respiratory variation indicates proper functioning of the tube. Limited changes in the level of the fluid in those drainage systems with a water column may indicate partial blockage. The tubing should be placed so that it does not coil, leaving low points to collect fluid. Such collections impede fluid flow and may cause positive pressure to build up in the tubing and back up into the patient. Air leakage is assessed by observing the water-seal chamber on the drainage device. Air leakage should be assessed on and off suction at quiet respiration. The patient is then asked to cough and the chamber is observed. Several grading systems have been devised. In general, air leaks should be characterized by the force necessary to produce the air leak and the amount of the air leak. The smallest leak is an intermittent one produced on inspiration only, and the largest one is a continuous air leak. Newer devices being evaluated currently display the amount of air leak digitally. Drainage should be measured twice daily, at least, so that an estimate can be made concerning whether the rate of fluid drainage is increasing or decreasing. Nurses usually record the drainage in 12-h shifts and provide a total daily drainage. In addition, the character of the drainage should be noted. Change in the character of the fluid from

sanguinous to serous is usually a good sign. Change from serous to purulent indicates potential empyema and a change to "milky" secretion a chylothorax. In planning the removal of a chest tube, the drainage must decrease to levels acceptable to the surgeon. Although exact numbers are not scientifically demonstrated, the amount is usually 200–300 mL/day or less. Chest tubes and drainage systems are intended to keep the lung expanded and prevent the development of a space. Once air leakage ceases and drainage has decreased to acceptable levels, the system has performed its function and should be removed. In an age of cost containment, this could be anytime after the operation, and usually is 2–4 days after a lobectomy.

We routinely use a preplaced U stitch to approximate the wound edges after chest tube removal. The chest tube is removed quickly during a breath hold at the end of expiration. The wound borders are brought together, and a wound dressing is applied. A chest radiograph must be obtained after to evaluate for adequate pulmonary reexpansion

Intravenous Fluids

Lung manipulation and collapse may impair pulmonary lymphatic drainage and increase extravascular lung water due to disruption of the alveolar-capillary membrane. Because of this, patients undergoing pulmonary resections should not receive excessive fluid replacement, and standard fluid management used in other types of surgical patients needs to be moderated. Excessive fluids can result in pulmonary edema, decreased alveolar gas permeability, decreased pulmonary compliance, atelectasis, and hypoxia.

An adult should receive not less than 1,000 mL of fluids per day. If there are no previous deficits or current complications, the typical amount of liquid ingested by an adult is 2–3.5 L/day. Two liters per day should maintain an adequate diuretic range (1,000 mL) and cover requirements for Na^+ , K^+ , and Cl^- . In special circumstances, such as after pneumonectomy or lung volume reduction surgery, more extreme fluid restriction (<1.5 L) may be advised. Attention needs to be given to how much fluid is provided with medications. Urine output and serum creatinine must be monitored very carefully, and medications need to be reviewed to reduce or eliminate other nephrotoxins, such as nonsteroidal antiinflammatory agents (NSAIDs) or angiotensin-converting enzyme inhibitors.

Postoperative Nutrition

The majority of patients start enteral nutrition in the evening of the day of surgery or the next day, unless they are hemodynamically unstable. Most patients tolerate limited postoperative nutrition for a week. Often overlooked is the early use of laxatives and stool softeners, which should be started on the first day with oral diet. Reduction of narcotics as tolerated, adequate oral hydration, and early ambulation help to overcome constipation.

Respiratory Care

Oxygen is administered as needed during the postoperative period. Chest physiotherapy has been demonstrated to be effective in preventing postoperative pulmonary complications and is considered routine postoperative care for patients undergoing thoracotomy. Many patients with hypoxemia benefit more from physiotherapy to increase functional residual capacity and PaO_2 than from further increases in the fraction of inspired oxygen (FiO_2). Excessive oxygen administration has potential drawbacks despite the short-term margin of safety it can provide. Increased alveolar oxygen tension promotes atelectasis as the oxygen is rapidly absorbed. Drying of secretions, even by humidified gases, can increase difficulty with coughing and clearance of mucus. Patients with COPD may have chronic carbon dioxide retention. Supplemental oxygen will tend to exacerbate hypercapnia in these patients. Therefore, in patients who have an elevated PaCO_2 preoperatively, oxygen saturation is maintained at 90% or less, preserving the hypoxic drive to breathe.

Early application of continuous positive airway pressure (CPAP) may prevent the need for intubation and mechanical ventilation in patients with hypoxemia by reducing atelectasis and, therefore, improving oxygenation. Clearing of secretions is very important after thoracic operations, especially after tracheal resections. In our institution we liberally use bronchoscopy and have a small bronchoscopy suite available on the thoracic surgery ward 24 h/day. Patients can be cleared of

secretions daily if their cough is ineffective. Alternatively a mini-tracheostomy can be placed via the cricothyroid membrane for tracheobronchial toilette, depending on institutional preference and experience.

Prevention of Venous Thromboembolism

Measures to prevent postoperative venous thromboembolism should be implemented in high-risk patients undergoing thoracic surgical procedures. The best method of prophylaxis is low-dose fractionated or unfractionated heparin. Pneumatic compression device are also used in some patients, although their role has never been formally demonstrated in randomized control trials. Risk for venous thromboembolic disease may be stratified according to patient and procedural factors. The majority of patients undergoing thoracic operation fit the high-risk category, as defined in Table 45.2. These patients have a calf thrombosis rate of 20–40%, a pulmonary embolus rate of 2–4%, and a fatality rate of 0.4–1.0%. In 2006, Mason et al. found a 7.4% incidence of postoperative venous thromboembolism among patients undergoing pneumonectomy for malignancy [7]. In 2007, the American Society of Clinical Oncology guidelines recommended that patients with cancer who will have a thoracotomy or laparoscopy lasting >30 min should receive pharmacologic thromboprophylaxis with either fractionated or unfractionated heparin. Prophylaxis should begin preoperatively or as early as possible in the

TABLE 45.2. Classification of risk levels for postoperative thromboembolism.

Thromboembolic event (%)		Calf vein thrombosis	Proximal vein thrombosis	Clinical pulmonary embolism	Fatal pulmonary embolism	Successful prevention strategies
Risk level						
Low		2	0.4	0.2	0.0002	No specific prophylaxis, early mobilization
Uncomplicated minor surgery in patients aged <40 years with no clinical risk factors						
Moderate		10–20	2–4	1–2	0.1–0.4	LDUH (q12h), LMWH ($\leq 3,400$ U daily), GCS or IPC
Any surgery in patients aged 40–60 years with no additional risk factors; major surgery in patients aged <40 years with no additional risk factors; minor surgery in patients with risk factors						
High		20–40	4–8	2–4	0.4–1.0	LDUH (q8h), LMWH ($>3,400$ U daily), or IPC
Major surgery in patients aged >60 years without additional risk factors or patients aged 40–60 years with additional risk factors; patients with myocardial infarction; medical patients with risk factors						
Highest		40–80	10–20	4–10	0.2–5.0	LMWH ($>3,400$ U daily), fondaparinux, oral VKAs (INR, 2–3), or IPC/GCS + LDUH/LMWH
Major surgery in patients aged >40 years with prior venous thromboembolism, malignant disease, or hypercoagulable state; patients with elective major lower extremity orthopedic surgery, hip fracture, stroke, multiple trauma, or spinal cord injury						

LDUH low-dose unfractionated heparin; LMWH low-molecular-weight heparin; GCS graduated compression stockings; IPC intermittent pneumatic compression; VKA vitamin K antagonist

Adapted from Geerts et al. [32]

postoperative period. A combined regimen of pharmacologic and mechanical prophylaxis may improve efficacy among the patients at highest risk.

General Complications of Thoracotomy

Pneumonia

Although the incidence is low, between 2.2 and 6%, pneumonia postthoracotomy contributes to significant morbidity. Risk factors include preoperative hospital stay, immuno-compromised status, procedure (pneumonectomy > lobectomy), pulmonary reserve, smoking, and atelectasis. Atelectasis is a common complication after pulmonary surgery, fortunately most is plate-like or linear, hence subsegmental, and has little consequence in a patient with adequate pulmonary reserve. However, segmental or lobar atelectasis may cause significant problems. Risk factors include poor cough, usually a result of poor pain control, impaired pulmonary function, chest wall instability, and/or sleeve resection.

Prevention is the best treatment. Chest physiotherapy with vibratory percussion, frequent spirometry exercises, and ambulation is key for prevention. Adequate pain control is also of paramount importance to prevent pneumonia. Whenever pneumonia is suspected sputum cultures or BAL, if a bronchoscopy is performed, should be obtained and broad-spectrum antibiotic therapy should be started. Clinical signs of pneumonia are a productive cough, fever, and/or an elevation in the white blood cell count. Radiographic findings often lag behind, especially in dehydrated patients.

Atrial Fibrillation

Arrhythmias are one of the most frequent complications after thoracic surgery. They require immediate management and often prolong the hospital stay. Because atrial arrhythmias are more common (ventricular arrhythmias are rare after thoracotomy) their management is specifically discussed here. The incidence of atrial tachyarrhythmias ranges from 3.8 to 37% after thoracic surgery, with atrial fibrillation (AF) being the most common arrhythmia [8]. It is commonly associated with respiratory complications. In a study by Bobbio et al. in 2007, there was a 30% incidence of AF in patients with either sputum retention, atelectasis, or pneumonia [9].

Many studies have been performed on the prevention of supraventricular tachyarrhythmias in patients undergoing lung resection. In a prospective randomized double-blind trial, Jakobsen et al. showed that administration of oral metoprolol initiated preoperatively and continued postoperatively decreased the incidence of AF from 40 to 6.7% [10]. In another trial, administration of magnesium sulfate starting the day of operative resection also resulted in a decrease in the incidence of AF from 26.7 to 10.7% [11]. Prophylactic oral amiodarone, when given before cardiac surgery, was

shown to be cost-effective and safe and might be a reasonable preventive strategy in thoracic or other noncardiac surgical patients [12]. The use of amiodarone has however been associated with acute lung injury in rare cases and must be used with caution after lung resection. There are currently no consensus guidelines for prevention of AF that is specific to thoracic surgical patients.

Dunning et al. on behalf of the European Association for Cardiothoracic Surgery Audit and Guidelines Committee published guidelines and suggested a treatment algorithm for postsurgical AF [13]. Once the diagnosis of an atrial tachyarrhythmia has been established, the first priority is to assess the patient's hemodynamic stability. In addition, one should maintain oxygenation, assess fluid balance, and assess the serum potassium. If the patient experiences syncope or if the blood pressure is less than 80 mmHg systolic, the options are chemical conversion, typically with amiodarone IV or synchronous electrical cardioversion. For electrical conversion, the first shock is typically delivered at 200 J, with subsequent shocks at 300 and 360 J, respectively.

If the patient is hemodynamically stable, one should achieve control over the ventricular rate to allow better ventricular filling and an optimal ejection fraction. In our institution, once the electrolytes (potassium, magnesium, and calcium) are corrected metoprolol would be the first choice except in patients with COPD and asthma. In this case our first choice is diltiazem. Amiodarone is usually a second choice in patients who are hemodynamically stable because of its potential pulmonary toxicity. Once rate control has been achieved, the medication may be changed to equivalent doses of oral medication over the next 24 h. Myocardial ischemia should be ruled out by electrocardiography. The natural history of postoperative atrial tachyarrhythmias is self-termination. Therefore, usually nothing more than a day or two of rate control is required. If the patient spontaneously converts to normal sinus rhythm over the next 24 h, the medication can be discontinued and no further treatment is required.

If, however, the patient remains in a rate-controlled fibrillation or flutter beyond 24 h, cardioversion can be attempted after echocardiography is performed to exclude the presence of intracardiac thrombus. Amiodarone has become the most popular drug for cardioversion, particularly since it is relatively safe in patients with depressed ventricular function. If the patient converts to sinus rhythm, the oral antiarrhythmic drug should be continued for at least 30 days after surgery.

If the arrhythmia persists for more than 48 h, the patient should be anticoagulated with heparin and then maintained on warfarin. Typically, if patients are discharged from the hospital in rate-controlled AF with adequate anticoagulation, they will spontaneously convert to sinus rhythm as outpatients. If, however, they remain in AF beyond 30 postoperative days, they should be offered outpatient electrical cardioversion provided that they have remained therapeutically anticoagulated.

Pleural Space Problems

It is important to have the remaining lung fully expanded to fill the chest cavity following thoracotomy. If this, for any reason, fails to happen, the space between the lung and the chest wall will fill with fluid. This might be the seed for an empyema. A postoperative space problem may occur when atelectasis of the underlying lung occurs or when an air leak from the lung leads to a persistent air space.

Air Leak

Not all patients have an air leak after pulmonary resection. In fact, many patients having a thoracoscopic wedge resection have no air leak. However, many patients having a lobectomy, segmentectomy, or a complicated wedge resection will leave the operating room with a leak. The STS Thoracic Surgery Database defined prolonged air leak as lasting >5 days. By August 2008, the database had recorded a total of 15,178 lobectomies. Of these patients, 9.6% had prolonged leaks. This complication was the second in frequency only after arrhythmia.

Factors increasing the incidence of a prolonged air leak include emphysema, bilobectomy compared to lobectomy, poor chest tube placement, and neglecting operative techniques that help prevent air leaks. These techniques include pleural tents, fissureless surgery, buttressed stapled lines, and checking for air leaks before closing.

However, if significant air leaks occur postoperatively, management varies. The old dictum of “no space, no problem” is a good one to keep in mind. When this is the case, the patient rarely requires intervention. When the lung does not fill the entire cavity and there is a significant air leak, a bronchopleural fistula (BPF) should be taken into consideration.

A BPF is defined as a communication between a bronchus and the pleural space and therefore different from an alveo-pleural fistula. The latter usually seals spontaneously with time, which is not the case for a BPF. Most commonly a BPF occurs following a right lower bi-lobectomy. This may be due to the lack of coverage of the bronchial stump by the remaining upper lobe because of the posterior inferior position of the stump. In other types of lobectomy the bronchial stump is well covered by the remaining lobes. Technical factors are responsible for fistulas occurring in the early postsurgical period. The most frequent errors are inappropriate suturing/stapling and ischemia produced by excessive dissection of the bronchus prior to closure. Prevention is the easiest way to manage BPF. Local tissue pedicle flaps such as pleura, azygos vein, pericardial fat, and intercostal muscle can be used to cover pneumonectomy or bi-lobectomy stumps. Treatment options for BPF are briefly discussed in the chapter empyema.

For patients with complete lung expansion and a prolonged air leak, the first question is whether the lung will stay expanded without suction and if the chest tube output is considered small. If both of these criteria are met, the chest tube

can be connected to a Heimlich valve or a similar device and the patient can be discharged with a close follow-up as an outpatient. This is a good strategy in patients having lung volume reduction surgery, a decidedly sick population with significant underlying lung disease [14]. Alternatively, there is the possibility of chest tube removal, even with a small air leak. Such a maneuver should be preceded by a trial of tube clamping for up to 6 h prior to removal. If the patient develops pulmonary symptoms, such as shortness of breath or hypoxia, or develops a pneumothorax, the tube can be unclamped and the procedure repeated another day. If the patient remains asymptomatic and no pneumothorax develops, the tube may be removed. A period of observation for 6–24 h is recommended prior to discharge. A last resort is to consider chemical pleurodesis. The instillation of sclerosing materials into the pleural space through the thoracostomy tube promotes symphysis of visceral and parietal pleura and may produce leak closure. Instillation of Doxycycline or talc has been described to treat a significant postoperative air leak [15].

Empyema

Empyema complicating lung resections is an uncommon but morbid and too often deadly sequela, particularly after pneumonectomy. Postsurgical empyema accounts for 20% of all cases of empyema. It most frequently follows a pneumonectomy, occurring in 2–7% of patients with a higher incidence for right pneumonectomy and it may occur in 1–3% of patients after lobectomy [16]. The incidence of empyema after pulmonary resection varies with the indications for the resection (inflammatory or neoplastic disease), with or without preoperative radiation.

Although empyema may occur at any time postoperatively, even years later, most empyema develop in the early postoperative period. The pleural space may be contaminated at the time of pulmonary resection with the development of a bronchopleural or esophago-pleural fistula or from blood-borne sources. After pulmonary resection that is less than a pneumonectomy, an empyema occurs more often when the pleural space is incompletely filled by the remaining lung. Risk factors for empyema are summarized in Table 45.3.

Symptoms and signs vary, but the possibility of an empyema must be considered in any patient with clinical features of infection after pulmonary resection. Expectoration

TABLE 45.3. Factors that increase the risk of development of post-surgical empyema.

Delay in diagnosis
Improper choice of antibiotics
Loculation or encapsulation by a dense inflammatory reaction
Presence of a bronchopleural fistula
Foreign body in the pleural space
Chronic infection
Entrapment of lung by thick visceral peel
Inadequate previous drainage or premature removal of a chest tube

of sero-sanguineous liquid and purulent discharge from the wound or the drain sites is almost always diagnostic. On radiography of the chest, usually a pleural opacity is seen, with or without a fluid level, when resection has been less than a pneumonectomy. After pneumonectomy, a decrease in the fluid level early postoperatively, or the appearance of a new fluid level when the pneumonectomy site was uniformly opaque, strongly suggests an infected pleural space with BPF (see Chap. 33, Fig. 33.17b). The pleural space should be immediately drained to prevent any contamination of the contra-lateral lung through the BPF and a bronchoscopy should be performed to determine the size and location of the defect in the bronchial stump. The timing of surgical intervention and the type of operative procedure undertaken to treat the BPF are tailored to the individual patient.

General treatment principles of postresectional empyema with or without a BPF include surgical drainage by closed chest tube insertion and institution of appropriate

antibiotic therapy. Once adequate drainage has been established and the remaining lung fills the chest without significant space and there is no underlying BPF, the course of management can be determined, usually within 10–14 days. If the patient has a persistent space without a BPF, the management depends on the size of the space.

Smaller spaces can be sterilized by irrigation with the appropriate antibiotic solution or fibrinolytic agents. Once the daily amount of drainage is <100 mL/day and no further collapse of the remaining lung develops if the tube is opened to atmospheric pressure, the tube can simply be removed, or closed drainage can be changed to open drainage by cutting it close to the chest wall (Fig. 45.2). The tube is then shortened at the rate of about 1 in. per week or until granulation tissue and fibrosis lead to its spontaneous expulsion from the pleural space. In certain cases, if the residual space is seen as too big a single-stage muscle flap closure of the remaining cavity can be performed. Larger spaces should be managed with an open

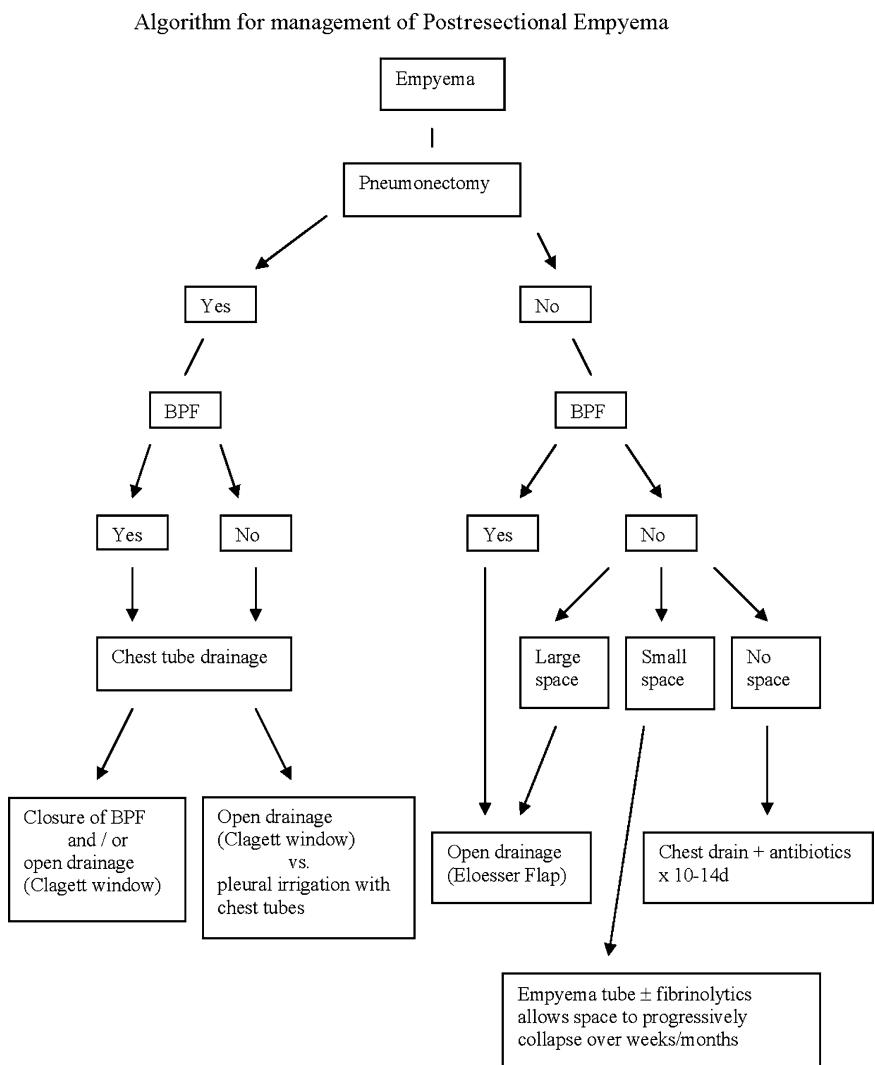


FIG. 45.2. Algorithm for management of postresectional empyema.

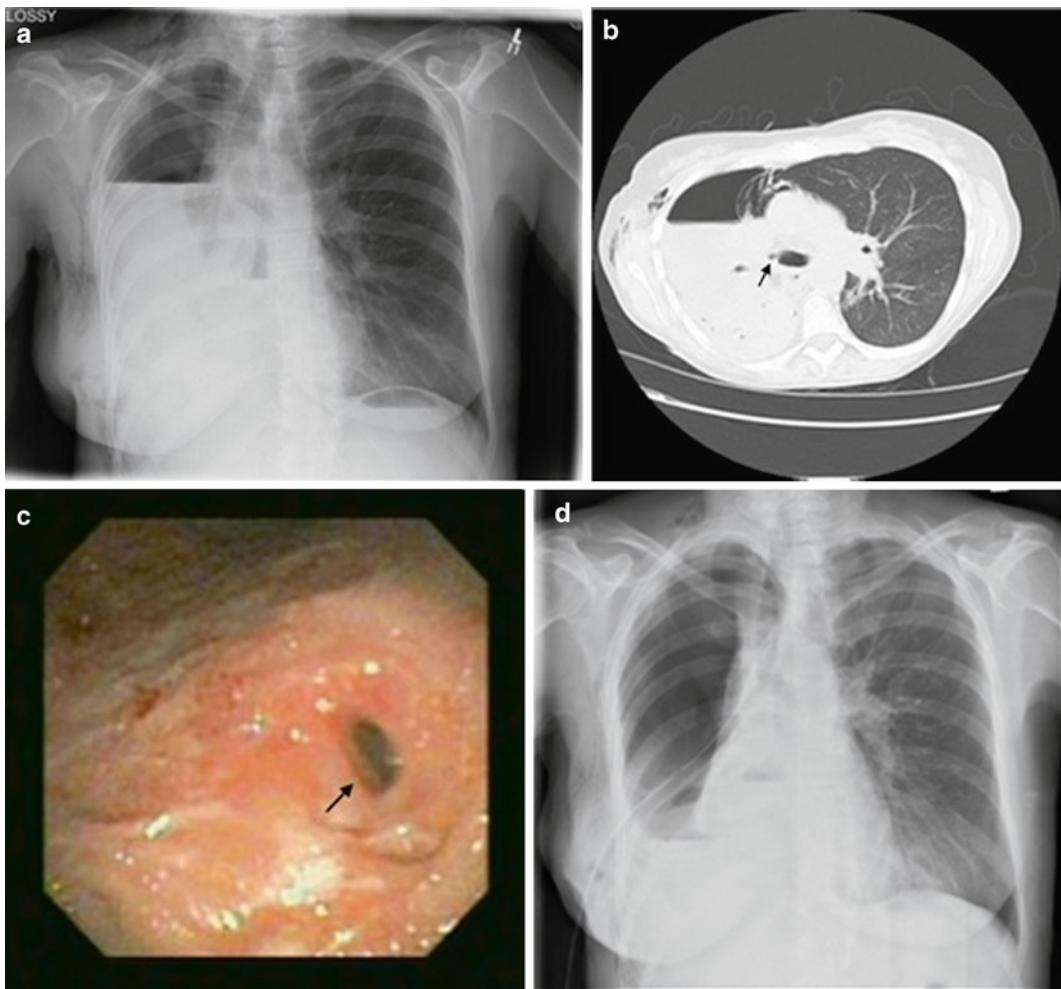


FIG. 45.3. Diagnosis and initial management of postpneumonectomy broncho-pleural fistula (BPF). (a) A chest X-ray 7 days after right pneumonectomy with the fluid level in the right chest almost reaching the carina. At this time the patient presented with a new onset of coughing. (b) A CT scan showed air in the mediastinum close to the bronchial stump (arrow) and subcutaneous emphysema (arrow), suspicious for a BPF. (c) A bronchoscopy confirmed the diagnosis of a BPF (arrow). (d) As initial treatment, a chest tube was inserted to drain the chest cavity and protect the left lung.

drainage, therefore we usually perform a modified Eloesser flap (see Chap. 33, Fig. 33.2).

If a BPF is present, the fistula should be closed by a myoplasty or omentoplasty followed by a single-stage muscle flap closure of the remaining space. In situations where the patient remains medically unstable after chest tube insertion or does not qualify for other medical reasons for the above-mentioned surgical procedure, the closed chest tube thoracostomy can be converted to open drainage with a Clagett window.

A postpneumonectomy empyema is associated with a BPF in approximately 40% of patients [17]. Significant factors contributing to the development of a BPF after pneumonectomy are induction chemo/radiotherapy, a right pneumonectomy, heavily calcified bronchial stump, positive surgical margin with cancer, and the need for postoperative

mechanical ventilation [18]. This can happen early in the postoperative course, usually by days 7–10, but can also manifest months after surgery. Initial goals in treatment are the prevention of contamination of the contra-lateral lung by closed tube drainage of the infected pleural cavity, taking in consideration that the mediastinum takes about 14 days until it is stable post pneumonectomy, institution of antibiotics, and a bronchoscopy (Fig. 45.3).

If no BPF is present a modified Clagett's procedure is performed. A second small chest tube is inserted into the second intercostal space, and a continuous inflow–outflow irrigation system is established through the pleural cavity. The irrigant is based on antibiotic sensitivities to the pleural drainage. This method achieves sterilization of the space in approximately 50% of patients. If the method is successful and the return

irrigant is negative by culture on 3 consecutive days after 2 weeks of irrigation, the chest tubes can be removed and pleural fluid is allowed to reaccumulate to fill the remaining space. If this method fails a Clagett window can be performed.

If a patient with postpneumonectomy empyema has a BPF, reinforcement of the bronchial stump with a healthy tissue flap (pericardial fat, intercostal muscle, etc.) should be achieved. If the fistula closes, one can attempt the aforementioned modified Clagett's sterilization of the cavity. In the patient in whom the BPF persists, the fistula and space are then managed by transposition of muscle flaps into the empyema space; this can be any extrathoracic muscle such as serratus anterior, latissimus dorsi, pectoralis major, or omentum. If the patient remains critical ill and unstable a Clagett window is ideal for long-term open drainage and irrigation. After the cavity is clean with granulating tissue, it can be closed.

Postpneumonectomy BPFs can cause major airway problems, especially in patients with respiratory failure. In case mechanical ventilation has to be used, the ventilation of the remaining lung may well be impossible due to loss of tidal volume through the fistula. Following a right pneumonectomy the endotracheal tube should be positioned distally in the left main bronchus with the cuff inflated. On the right side this can be a much greater problem since cuff inflation in the right main bronchus usually produces obstruction of the right upper lobe bronchus. High-frequency oscillatory ventilation (HFOV) may be useful in this circumstance. An algorithm of the surgical management of postresectional empyema is shown in Fig. 45.2.

Nerve Injury

Injury to the recurrent laryngeal nerve can occur during right- or left-sided thoracic surgery procedures. The left nerve is far more in danger to be injured than is the right. Its position under the aortic arch makes it susceptible to injury during any procedure in this area. The nerve is, on occasion, "sacrificed" intentionally, if radical resection for a tumor known to involve the vagus nerve is required. The incidence ranges somewhere between 4 and 45% according to the type of procedure performed [19].

The patients with injury to the recurrent laryngeal nerve generally present in the postoperative phase with a weak and whispery voice, although cord edema in the very early postextubation period may mask the hoarseness. However, patients with palsy or paresis of the recurrent nerve have symptoms lasting well beyond the postoperative period. Those with paresis may describe a normal voice in the morning that becomes weaker over the course of the day. This may result in a weak cough or aspiration after drinking, leading to poor pulmonary physiotherapy and recurrent pneumonia. At laryngoscopy, adduction of the affected vocal cord will be absent or sluggish. Treatment involves determining the extent of injury and whether the injury is transient or permanent. A thorough evaluation of the significance of the cord should be done by fiberoptic evaluation of swallowing and sensation.

To assist with pulmonary physiotherapy and decrease the risk of aspiration, medialization laryngoplasty may be suggested. This can be done with the aid of autologous fat, Gelfoam, collagen, or polytetrafluoroethylene (PTFE). These are usually temporary solutions. A permanent solution involves medialization of the vocal cord by thyroplasty [20].

Injury to the phrenic nerve can occur in both open and thoracoscopic pulmonary resections. The most common causes are adherence of the lung to the pericardium or injuries occurring during performance of resection of anterior mediastinal tumors, resection of superior sulcus tumors, repair of thoracic outlet syndrome, or right-sided mediastinal lymph node dissection. Such injuries may be temporary or permanent. In a spontaneously breathing patient the diagnosis can be easily made by a chest radiographs demonstrating elevation of the affected hemidiaphragm. If the patient requires postoperative ventilation this radiographic finding might not be present due to positive pressure ventilation keeping the diaphragm in a fairly normal position. Depending on the severity of their underlying pulmonary disease, these patients may be difficult to wean from the ventilator. Phrenic nerve palsy can contribute to significant postoperative morbidity and symptoms according to the underlying pulmonary status of the patient. Diaphragmatic plication is indicated for symptomatic relief of dyspnea [21].

Postoperative Hemorrhage

The incidence of significant postoperative bleeding after a pulmonary resection requiring at least four units of packed red blood cells was identified to be 2.9% after lobectomy and 3.0% after pneumonectomy [22]. Chest tube output exceeding 1,000 mL over 1 h or persistent bleeding over 200 mL/h for 4–6 h after a pulmonary resection mandates reexploration, assuming that the coagulation parameters are corrected. Bleeding may stem from mediastinal or bronchial vessels (23%), intercostal vessels (17%), or a pulmonary vessel (17%); in the majority of cases (41%), no source of the hemorrhage is identified [23]. Such troublesome postoperative bleeding is particularly prone to occur if there has been a previous thoracotomy, a decortication of parietal and visceral "peel" due to empyema or resections for inflammatory disease such as old tuberculosis or aspergillosis. With multiple bleeding sites present on the chest wall it might be necessary for the surgeon to pack the pleural space for a period of time prior to closure of the thoracotomy. This may be particularly useful when the remaining lung fails to fill the pleural space or after pneumonectomy.

Chylothorax

A chylothorax is diagnosed when a "milky" effusion is drained through the chest tube once the patient is on enteral intake. However, if the patient has been fasting after resection, the characteristic creamy color of the effusion may not be noted.

In this case a persistent high chest tube output for unknown reason makes this diagnosis suspicious. The incidence of chylothorax after pulmonary resection is between 0.04 and 2% [24]. Etiologies include aggressive mediastinal lymph node dissection with incomplete ligation of lymphatic channels or direct injury to the thoracic duct [25]. The diagnosis is made by sending the pleural fluid for analysis. A triglyceride level >110 mg/dL, a lymphocyte count $>90\%$, and the presence of chylomicrons help to confirm the diagnosis [26].

A trial of conservative management is initially recommended, with the objective of adequately draining the pleural space, reexpanding the remaining lung, and keeping the patient fasting. The patient should be strictly NPO and be fed by parenteral nutrition. Occasionally medium-chain triglyceride (MCT) diet has been successfully used to stop the leak. Waiting for 7 days is normally advocated. It is generally agreed that a continuous chyle leak in excess of ≥ 1 L/day in a patient with complete cessation of oral intake is an indication for reoperation. Attempts at direct repair of the lymphatic injury often fail because of the difficulty of identifying and suturing the injury. Operative ligation of the thoracic duct low in the right chest is appropriate, and the success of thoracic duct ligation is 91%. Other options have been described for management of chylothorax after pulmonary resection. Pleuroperitoneal shunt has resulted in the resolution of chylothorax in some series [27]. Another option, rarely used because of the technical difficulty, includes the use of a pleural-venous shunt or percutaneous catheterization of the thoracic duct and embolization [28].

Torsion of a Residual Lobe

Lobes of the lung are usually held in their position by the other lobes, the inferior pulmonary ligament and incomplete fissures. After lobectomy these structures no longer exist. In particular, the middle lobe and lingula are most susceptible for torsion following a right upper lobectomy or a lingula sparing left upper lobectomy, respectively. Lobar torsion typically presents early in the postoperative period with fever, tachycardia, and loss of breath sounds on the affected side. Often the clinical picture is not impressive. Chest X-ray can demonstrate atelectasis of the torse lobe. Bronchoscopy should be done urgently to make the diagnosis, followed by urgent surgical exploration. The bronchoscopy will show a fish-mouth orifice to the lobe, which easily admits the bronchoscope. If the torsion is discovered early enough, the lobe may be preserved by untwisting the hilum. Most often, however, lobectomy is required. The incidence of lobar torsion after pulmonary resection is between 0.09 and 0.3% [29]. Lobar torsion of the middle lobe after a right upper lobectomy accounted for 70% of the cases in the literature. To prevent this complication, fixation of the middle lobe with the lower lobe may be performed in situations where the oblique fissure is complete.

Postpneumonectomy Syndrome

In a small number of patients undergoing pneumonectomy, mediastinal shift and rotation toward the empty hemithorax may cause pulmonary symptoms. This typically occurs in children or young adults. Along with the shift of the mediastinal contents, there is over-distention and herniation of the remaining lung. This results in dynamic airway compression of the left main bronchus between the left pulmonary artery and aorta after a right pneumonectomy or compression of the right main bronchus between the right pulmonary artery and the thoracic spine after left pneumonectomy. The overall incidence is not clear. Patients typically present with dyspnea, stridor, and recurring pneumonia, which may occur weeks to years after pneumonectomy. Diagnosis is made from chest radiographs, computed tomography scans, and bronchoscopy under conscious sedation demonstrating dynamic obstruction of the bronchus. Repositioning of the mediastinum and placement of a saline-filled tissue expander in the postpneumonectomy space is the treatment of choice [30].

Cardiac Herniation

Cardiac herniation rarely occurs but can be fatal in certain circumstances and therefore requires a high degree of suspicion. If the pericardium is opened widely or removed the heart is held in place by the lungs on both sides. If a major portion of the lung is removed the heart finds a space in which it may herniate. On the right side herniation can be life-threatening in a matter of minutes because both vena cavae would be strangulated by a 180° rotation of the heart into the right pleural space. On the left side the heart is freely suspended by the major vessels and risk of inflow- and outflow occlusion is not present. A greater problem is a moderate size defect in the pericardium through which the heart can herniate and subsequently become compromised by postoperative edema.

To avoid these scenarios a simple closure of the pericardial defect can be performed for smaller lesions, while larger defects should be closed with a fenestrated mesh [31]. Simple suture closure of larger defects may lead to cardiac tamponade.

The diagnosis of cardiac herniation might not be easy to make, especially for left-sided herniation. Symptoms include the sudden onset of low cardiac output and signs of central venous obstruction. If time is available, a chest radiograph will be diagnostic. Management of these patients includes emergent operative intervention with reduction of the cardiac hernia and patch closure of the defect using PTFE. Since PTFE is watertight, fenestrations must be created.

Clinical Case Discussion

A 70-year-old female has a right completion pneumonectomy and partial excision of the right chest wall for nonsmall cell lung cancer. Thirty years before the patient had a

right upper lobectomy for tuberculosis. The patient is 52 kg and 160 cm, FEV 1=64%, DLCO=60%, V/Q scan perfusion L:R is 65:35, good exercise tolerance, Hb is 124 g/dL, and other laboratory examinations including transthoracic echo-cardiography are normal. The anesthetic is with a combined T4–5 thoracic epidural and general anesthesia. The operative duration is 4 h. The blood loss is 500 mL. The patient receives 1 L of ringers lactate and 500 mL of synthetic isotonic colloid intravenously during the case. One R chest drain is placed and connected to an underwater-seal drainage system without suction. The patient is extubated in the operating room awake and comfortable and transferred to the recovery room in stable condition: heart rate 90/min, BP 100/50, CVP 4 mmHg, and urine output 30 mL/h. The thoracic epidural infusion is bupivacaine 0.1% with 15 µg/mL hydromorphone at 5 cc/h.

After 2 h in the recovery room the patient's HR has gradually increased to 110, the BP has decreased to 90/50, CVP remains 4 mmHg, and the urine output has fallen to 15 mL/h. Repeat Hb is 103 g/dL. The chest tube is fluctuating normally with respiration and there has been no significant drainage from the right chest. The patient receives repeat boluses of 500 mL ringers lactate $\times 2$ intravenously. One hour later the hemodynamics have not improved, she has a demonstrable sensory block from T2–10 without motor block. The thoracic epidural infusion is decreased to 2 mL/h. One hour later the patient is complaining of 5 out of 10 incisional pain and there is no demonstrable sensory or motor block. The HR is 115/min. BP 78/50, CVP 4, Hb 98 g/dL and urine output 10 mL/kg. Arterial blood gases are normal. What is the most appropriate next step?

1. Transfuse 500 mL of colloid.
2. Discontinue the epidural and begin intravenous PCA opioid analgesia.
3. Repeat the chest X-ray.
4. Obtain an ECG.
5. Obtain CT contrast pulmonary angiography.
6. Return to the operating room for cardiac herniation.

The most important postpneumonectomy complication to rule out in this context is cardiac herniation (see also Chap. 41) since it is so treatable and so lethal if not treated promptly. Cardiac herniation after a right pneumonectomy is most likely to present as a sudden onset of severe life-threatening hypotension. That is not the presentation in this case so there is time to confirm the diagnosis. The repeat chest X-ray 4 h postop. is shown in Fig. 45.4. An unrelieved negative pressure has developed in the right-chest due to the one-way valve effect of the underwater-seal chest drain. The mediastinal shift to the right created symptoms equivalent to a herniation with compromise of the venous return to the right-heart. The tip of the CVP catheter was at the SVC-right atrial junction and thus was downstream



FIG. 45.4. Chest X-ray of a 70-year-old female 4 h postop. after a right completion pneumonectomy and partial excision of the chest wall. The chest tube was connected to an under-water seal drainage system which allowed the development of an excessive negative intrathoracic pressure causing a complete shift of the mediastinum to the right lateral chest wall and compromise of the venous return to the heart.

from the venous inflow obstruction and accurately reflected the decreased filling pressures of the right-heart, but not the systemic venous volume. The mediastinum was “balanced” by injecting 500 mL of air into the right chest tube which was then clamped (Fig 45.5). The patient's hemodynamics rapidly returned to normal, the epidural infusion was increased to control the pain and the chest drain was removed the next day.

The presence of a functioning, normally fluctuating, chest drain in this patient makes the possibility of a tension pneumothorax or massive hemorrhage into the operative hemithorax very unlikely. Epidural local anesthetic overdosing is unlikely with the regression of the sensory block. Myocardial ischemia and pulmonary embolus must be considered in the differential diagnosis of postoperative hypotension, but are not specific complications related to pneumonectomy. The different options for chest drain management after a pneumonectomy are explained in section “Chest Drainage System.”

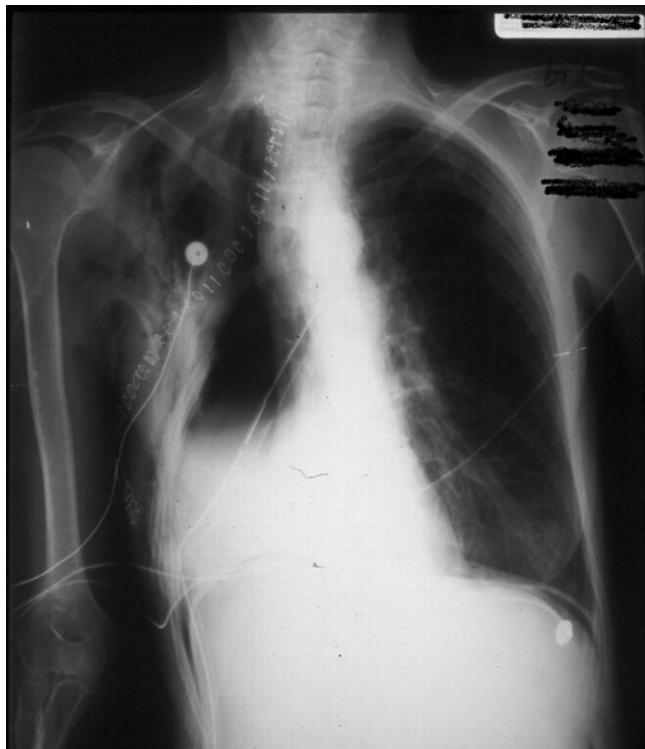


FIG 45.5. Chest X-ray of the same patient after 500 mL of air was injected via the chest drain which was then clamped. The mediastinum has been “balanced” which relieved the obstruction of venous inflow to the right heart and allowed the hemodynamics to return to normal.

References

1. Wright CD et al. Pulmonary lobectomy patient care pathway: a model to control cost and maintain quality. *Ann Thorac Surg*. 1997;64:299.
2. Gracey DR, Divertie MB, Didier EP. Preoperative pulmonary preparation of patients with chronic obstructive pulmonary disease: a prospective study. *Chest*. 1979;76:123.
3. Debigare R et al. Feasibility and efficacy of home exercise training before lung volume reduction. *J Cardiopulm Rehabil*. 1999;19:235.
4. Anthonisen NR et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV₁: the Lung Health Study. *JAMA*. 1994;272:1497.
5. Nakagawa M, Tanaka H, Tsukuma H, et al. Relationship between the duration of the preoperative smoke-free period and the incidence of postoperative pulmonary complications after pulmonary surgery. *Chest*. 2001;120:705.
6. Barrera R. Smoking and timing of cessation: impact on pulmonary complications after thoracotomy. *Chest*. 2005;127:1977.
7. Mason DP, Quader MA, Blackstone EH, et al. Thromboembolism after pneumonectomy for malignancy: an independent marker of poor outcome. *J Thorac Cardiovasc Surg*. 2006;131:711–8.
8. Rena O, Papalia E, Oliaro A, et al. Supraventricular arrhythmias after resection surgery of the lung. *Eur J Cardiothorac Surg*. 2001;20:688–93.
9. Bobbio A, Caporale D, Internullo E, et al. Postoperative outcome of patients undergoing lung resection presenting with new-onset atrial fibrillation managed by amiodarone or diltiazem. *Eur J Cardiothorac Surg*. 2007;31:70–4.
10. Jakobsen CJ, Bille S, Ahlborg P, et al. Perioperative metoprolol reduces the frequency of atrial fibrillation after thoracotomy for lung resection. *J Cardiothorac Vasc Anesth*. 1997;11:746–51.
11. Terazi A, Furlan G, Chiavacci P, et al. Prevention of atrial tachyarrhythmias after non-cardiac thoracic surgery by infusion of magnesium sulfate. *Thorac Cardiovasc Surg*. 1996;44:300–3.
12. White CM, Giri S, Tsikouris JP, et al. A comparison of two individual amiodarone regimens to placebo in open heart surgery patients. *Ann Thorac Surg*. 2002;74:69–74.
13. Dunning J et al. Guidelines on the prevention and management of de novo atrial fibrillation after cardiac and thoracic surgery. *Eur J Cardiothorac Surg*. 2006;30:852.
14. McKenna Jr RJ, Fischel RJ, Brenner M, Gelb AF. Use of the Heimlich valve to shorten hospital stay after lung reduction surgery for emphysema. *Ann Thorac Surg*. 1996;61:1115–7.
15. Kilic D, Findikcioglu A, Hatipoglu A. A different application method of talc pleurodesis for the treatment of persistent air leak. *Aust N Z J Surg*. 2006;76:754–6.
16. Deschamps C, Bernard A, Nichols III FC, et al. Empyema and bronchopleural fistula after pneumonectomy factors affecting incidence. *Ann Thorac Surg*. 2001;72:243–7.
17. Cerfolio RJ. The incidence, etiology, and prevention of postresectional bronchopleural fistula. *Semin Thorac Cardiovasc Surg*. 2001;13:3–7.
18. Hollaus PH, Setinek U, Lax F, et al. Risk factors for bronchopleural fistula after pneumonectomy: stump size does matter. *Thorac Cardiovasc Surg*. 2003;51:162–6.
19. Krasna MJ, Forti G. Nerve injury: injury to the recurrent laryngeal, phrenic, vagus, long thoracic, and sympathetic nerves during thoracic surgery. *Thorac Surg Clin*. 2006;16:267–75.
20. Schneider B, Schickinger-Fischer B, Zumtobel M, et al. Concept for diagnosis and therapy of unilateral recurrent laryngeal nerve paralysis following thoracic surgery. *Thorac Cardiovasc Surg*. 2003;51(6):327–31.
21. Simansky DA, Paley M, Rafaeli Y, Yellin A. Diaphragm plication following phrenic nerve injury: a comparison of paediatric and adult patients. *Thorax*. 2002;57:613–6.
22. Harpole Jr DH, DeCamp Jr MM, Daley J, et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg*. 1999;117:969–79.
23. Sirbu H, Busch T, Aleksic I, et al. Chest re-exploration for complications after lung surgery. *Thorac Cardiovasc Surg*. 1999;47:73–6.
24. Kutlu CA, Sayar A, Olgac G, et al. Chylothorax: a complication following lung resection in patients with NSCLC: chylothorax following lung resection. *Thorac Cardiovasc Surg*. 2003;51:342–5.
25. Haniuda M, Nishimura H, Kobayashi O, et al. Management of chylothorax after pulmonary resection. *J Am Coll Surg*. 1995;180:537–40.
26. Agrawal V, Doecken P, Sahn SA. Pleural fluid analysis in chylous pleural effusion. *Chest*. 2008;133:1436–41.
27. Murphy MC, Newman BM, Rodgers BM. Pleuroperitoneal shunts in the management of persistent chylothorax. *Ann Thorac Surg*. 1989;48:195–200.
28. Itkin M, Kucharczuk JC, Kwak A, Trerotola SO, Kaiser LR. Nonoperative thoracic duct embolization for traumatic thoracic

- duct leak: experience in 109 patients. *J Thorac Cardiovasc Surg.* 2010;139(3):584–90.
29. Cable DM, Deschamps C, Allen MS, et al. Lobar torsion after pulmonary resection: presentation and outcome. *J Thorac Cardiovasc Surg.* 2001;122:1091–3.
30. Shen KR, Wain JC, Wright CD, et al. Postpneumonectomy syndrome: surgical management and long-term results. *J Thorac Cardiovasc Surg.* 2008;135:1210–6.
31. Sugarbaker DJ, Jaklitsch MT, Bueno R, et al. Prevention, early detection, and management of complications after 328 consecutive extrapleural pneumonectomies. *J Thorac Cardiovasc Surg.* 2004;128:138–46.
32. Geerts WH et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest.* 2004;126:338S.

Pain Management After Thoracic Surgery

Stephen H. Pennefather and James McKeith

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Key Points

- Thoracic surgery can cause significant pain and suffering. Appropriate analgesia is important both for humanitarian reasons and to allow early mobilisation and pulmonary rehabilitation. Poor pain relief can increase pulmonary complications and mortality.
- Pain after thoracic surgery is generated from multiple structures and is transmitted via a number of afferent pathways. Factors that affect pain post-operatively can be divided into patient factors, analgesic technique and surgical approach.
- Paravertebral catheters and thoracic epidural analgesia are widely used for thoracotomies and both have advantages and disadvantages. The optimal solutions for thoracic epidurals contain a low dose local anaesthetics combined with a lipophilic opioid. Paravertebrals with higher doses of local anaesthetic are more efficacious. Further direct comparisons between the two techniques are required to establish the role of each option.
- Opioid tolerant patients pose a particular challenge. Maintenance opioid should be continued peri-operatively to avoid withdrawal symptoms. A regional technique, supplemented with non-opioid analgesics is advised.

Introduction

A posterolateral thoracotomy is amongst the most painful incisions and thus unsurprisingly patients can, and sometimes do, suffer considerable pain in the post-operative period if analgesia is not managed appropriately. Poorly treated post-thoracotomy pain greatly reduces patient satisfaction, their quality of life and sometimes the quality of life of their loved ones. Under-treated pain can also reduce the patient's ability to co-operate with post-operative physiotherapy and remobilisation. The effectiveness of post-thoracotomy pain control can perhaps best be determined by assessing the patient's ability to participate in post-operative physiotherapy and other rehabilitation regimens. Effective pain control can facilitate a reduction in post-operative complications, particularly post-operative pulmonary complications. Over the years a large number of drugs, combinations of drugs and techniques to deliver these drugs have been developed and used to control post-thoracotomy pain. Unfortunately, no technique has emerged that is safe, effective and applicable to all patients. Until the early 1980s, systemic opioids formed the mainstay of post-thoracotomy analgesia in the West. Thoracic epidurals were introduced into clinical practice for post-thoracotomy

analgesia in the mid-1970s [1, 2] and had become the gold standard of post-thoracotomy analgesia by the mid-1990s [3]. Somatic paravertebral blocks are now gaining acceptance as an alternative method for providing post-thoracotomy analgesia. A number of factors have led to the increased use of somatic paravertebral blocks. The risks associated with the peri-operative use of epidural analgesia are becoming clearer and are perhaps greater than previously thought [4, 5]. More patients are presenting for thoracic surgery on multiple anti-platelet agents sometimes with intra-coronary stents in situ. While dual antiplatelet therapy is known to be a contraindication to thoracic epidural analgesia [6] the risk of discontinuing antiplatelet agents peri-operatively is now quantifiable [7–9].

FIG. 46.1. A meta-analysis of trials comparing paravertebral block with thoracic epidural analgesia on postoperative pulmonary complications (reproduced from Davies et al. [11] by permission of Oxford University Press).

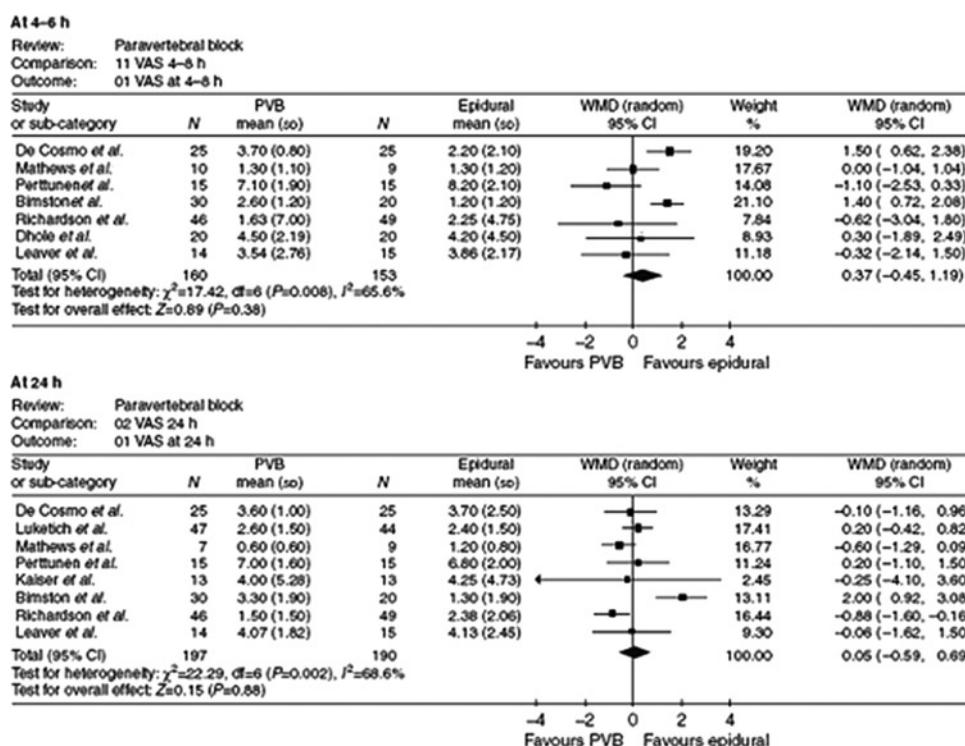
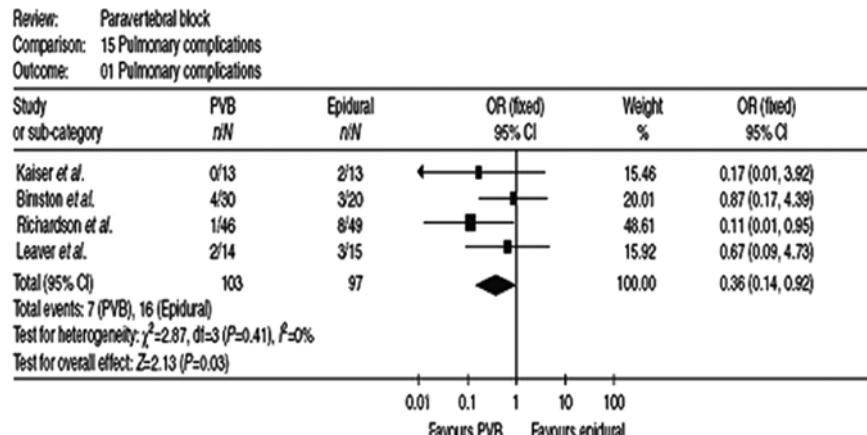


FIG. 46.2. A meta-analysis of trials comparing paravertebral block with thoracic epidural analgesia on visual analogue pain scores (reproduced from Davies et al. [11] by permission of Oxford University Press).

Few randomised studies have compared outcomes after thoracic epidural analgesia or paravertebral block. The limited results available, however, suggest that paravertebral blocks may be more effective at reducing respiratory complications than thoracic epidural analgesia and after the first few hours provide equivalent analgesia [10, 11] (see Figs. 46.1 and 46.2).

Well-informed patients may experience less pain [12] so whenever possible patients should receive a full explanation of the proposed analgesic technique and its likely effects including its limitations, potential side effects and incidence of complications. The relative merits of the alternative strategies should also be discussed. How much to tell patients about potential

complications remains controversial. There is, however, a trend towards more openness. The understanding of informed consent has shifted with time. In the United Kingdom, at least, the standard is no longer what a body of reasonable practitioners would do but what a reasonable patient would expect. In 2001, the position was summarised “as part of the process of obtaining consent, except when they have indicated otherwise, patients should be given sufficient information about what is to take place, the risks, uncertainties, and possible negative consequences of the proposed treatments, about any alternatives and about the likely outcome, to enable them to make a choice about how to proceed” [13]. This change in the standard has resulted in a change in practice. Most anaesthetists now, for example, take specific consent for thoracic epidural analgesia [14]. Acute post-thoracotomy pain management aims to reduce the patient’s pain as much as possible but to do so safely. In practice most patients undergoing thoracic surgery can be safely and effectively managed by thoracic epidural analgesia, paravertebral blocks or systemic opioids supplemented when appropriate by other systemic analgesics.

Pathophysiology of Post-thoracotomy Pain

The pathogenesis of post-thoracotomy pain is complex. Nociceptive receptors are stimulated by the skin incision, division and retraction of the muscles, retraction and sometimes fracture of ribs. In addition, ligaments may be stretched, costochondral joints dislocated and intercostal nerves injured, causing further pain. The incised pleura are frequently irritated by partial surgical stripping, chest drains and residual pleural blood; the resulting inflammatory responses activate further nociceptors. The central transmission of these multiple nociceptive signals amplifies pain transmission and increases pain perception through central sensitisation (see Fig. 46.3).

Without adequate treatment post-thoracotomy pain can be very severe and has been rated as near the top of a league of iatrogenic causes [15]. The surgical wound is subject to continuous movement as the patient breathes and ventilation is adversely affected. Inspiration stretches the injured structures initiating a reflex contraction of the expiratory muscles. Splinting of the injured hemi-thorax occurs to limit the distraction of the injured structures. Similarly, the usually passive expiration becomes active. Functional residual capacity falls usually to below the closing capacity and airway closure occurs. This can result in atelectasis, shunting and hypoxaemia. Deep inspiration is limited by pain, forced expiratory flow is thus reduced and effective coughing impaired. Sputum clearance is often adversely affected. Effective analgesia can reverse some of these changes and improve pulmonary function post-thoracotomy. There are, however, many other causes for the deterioration in pulmonary function that occurs post-thoracotomy. To date it has not been possible to determine with any accuracy the relative importance of pain in the aetiology of the changes in pulmonary function seen post-thoracotomy (see Table 46.1).

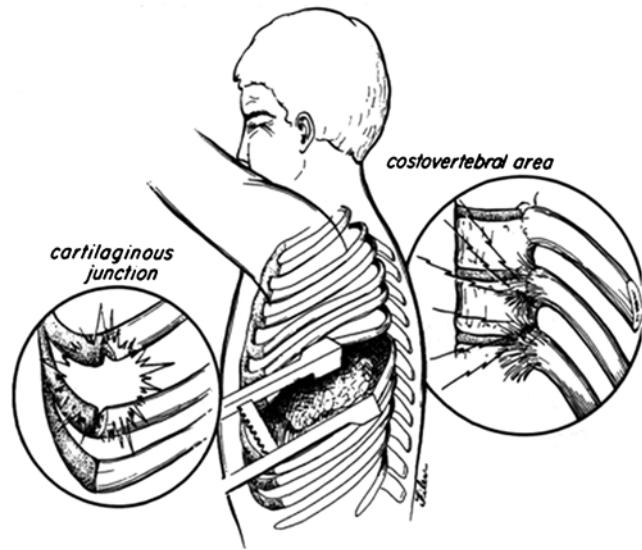


FIG. 46.3. Direct injury to ribs and neurovascular intercostals bundle along with injuries to anterior and posterior intercostals articulations during a thoracotomy (this figure was published in Landreneau et al. [276]. © Elsevier [1994]).

TABLE 46.1. Causes for deterioration in pulmonary function post-thoracotomy.

- Lung tissue resection
- Haemorrhage and oedema in residual lung tissue
- Distortion in bronchial architecture with resultant lobar collapse
- Gastric and abdominal distension
- Increased airway resistance
- Impaired mucociliary clearance
- Residual effects of anaesthesia
- Pain related changes in lung mechanics
- Diaphragmatic dysfunction

Reproduced with permission from Pennefather and Russell [279].

There are a number of mechanisms for transmitting the pain, generated post-thoracotomy, to the sensorium: Stimuli from the chest wall, costal and peripheral diaphragmatic pleura are transmitted via the intercostal nerves. Stimuli from the pericardium and mediastinum are transmitted via the phrenic nerve. In addition, the vagus nerve contains somatic and visceral afferent nerve fibres and blockade of the vagus nerve has been advocated during thoracic surgery [16]. The sympathetic nerves may play a role in transmitting pain from the lung and mediastinum. It has been suggested that stretching of the brachial plexuses and distraction of the shoulder contributes to the pain in some patients [17].

Recent work has improved the understanding of mechanisms of post-thoracotomy pain. The phrenic nerve supplies sensory branches to the mediastinal pleura, to the fibrous pericardium, the parietal layer of the serous pericardium and diaphragmatic dome pleura. While well-managed thoracic epidurals provide excellent post-thoracotomy analgesia in the somatic dermatomes most patients still experience ipsilateral shoulder pain [18, 19]. In patient’s receiving thoracic epidural

analgesia, the intra-operative blocking of the phrenic nerve at the level of the pericardial fat pad with local anaesthetic prevents ipsilateral shoulder pain in most, but not all patients [19]. Branches of the phrenic nerve to the pericardium or mediastinum arising proximal to the pericardial fat pad may account for the shoulder pain in some of the remaining patients. Supporting this hypothesis is the observation that patients in the above study who had undergone an intra-pericardial pneumonectomy and received a phrenic nerve block still experienced shoulder pain. An accessory phrenic is an alternative explanation. The ability of a combined phrenic nerve block and thoracic epidural to almost eliminate early post-thoracotomy pain [19] suggests that the contribution of the vagus nerve to post-thoracotomy pain may be minimal. In contrast, human vagal nerve stimulation can suppress pain [20]. Blocking the vagus nerve might actually increase post-thoracotomy pain by reducing vagally mediated central inhibition of pain.

Factors Influencing Pain After Thoracic Surgery

Pre-operative Preparedness

Well-informed patients may experience less pain [12] so whenever possible patients should receive a full explanation of the proposed analgesic technique and its likely effects including its limitations, potential side effects and complications.

Opioid Tolerance

Continuous opioid exposure results in a rightward shift of the dose-response curve to opioids resulting in patients requiring increased amounts of opioid to obtain the same pharmacological effect. It is a predictable pharmacological adaptation [21]. The degree of opioid tolerance is related to the dosage, duration and type of opioid administered. Opioid tolerance probably occurs because of decreased opioid receptor sensitivity and density [22], up-regulation of cyclic adenosine monophosphate [23] and neural adaptation [24]. Activation of *N*-methyl-D-aspartate (NMDA) receptors plays an important role in the development of opioid tolerance [25]. Opioid tolerant patients are relatively pain intolerant [26] and may have greater difficulty in coping with acute pain [27].

Pre-emptive Analgesia

The concept of pre-emptive analgesia was first suggested by Crile [28] although modern clinical interest is largely the result of basic science research done by Woolf [29]. Pre-emptive analgesia is anti-nociceptive treatment started before the noxious stimulus that aims to prevent the establishment of altered central processing of sensory input that amplifies post-operative pain [30]. Pre-emptive analgesia aims to decrease

acute post-operative pain, even after the analgesic effects of the pre-emptive drugs have worn off, and to inhibit the development of chronic post-operative pain. Potential candidates for patients undergoing a thoracotomy include pre-incisional thoracic epidurals, paravertebral blocks, NMDA antagonists, gabapentin and systemic opioids. Although the results of clinical studies to support the concept of initiating the pain treatment prior to the injury are conflicting there is widespread belief in the concept amongst clinicians. A 2002 systematic review of pre-emptive analgesia for post-operative pain relief found no evidence of benefit for the pre-emptive administration of systemic opioids, non-steroidal anti-inflammatory drugs (NSAIDs) or ketamine and little evidence of benefit with continuous epidural analgesia [31]. A 2005 systemic review on the impact of pre-emptive epidural analgesia on pain after thoracotomy concluded that pre-emptive thoracic epidural analgesia was associated with a reduction in acute pain but no reduction in chronic post-thoracotomy pain [32].

Sex

A considerable amount of work has been undertaken in an attempt to determine the influence of the sex of the patient on the pain experienced after surgery. Female patients report pain to be more severe, frequent and diffuse than male patients with similar disease processes [33]. A meta-analysis of the influence of sex differences in the perception of noxious experimental stimuli, found that females were less tolerant of noxious stimuli than males [34]. The difference in pain perception between males and females decreases with age [35], has not been found by all investigators and is usually only moderately large. Social gender roles have a significant influence on pain tolerance levels [36], are sometimes difficult to differentiate from the sex of the patient and may account for some of the differences in pain tolerance between the sexes. Coping strategies also influence patient's pain tolerance; catastrophizing is associated with an increased sensitivity to experimental pain [37]. Women are more likely to catastrophize and this may help account for the differences in pain tolerance between the sexes [38]. Anaesthetists should be aware of the different responses male and female patients have to pain but as yet no specific recommendation with respect to treatment can be made.

Age

A recent systematic review found young age to be a significant predictor of post-operative pain [39]. The pharmacokinetics of analgesic drugs can be affected by ageing and the elderly are considered to be more sensitive to systemic opioids [40]. Similarly, there is a positive correlation between age and thoracic epidural spread with elderly patients requiring about 40% less epidural solution [41, 42]. It has also been suggested that age blunts peripheral nociceptive function decreasing

pain in some contexts [43] although this is not the experience of at least one ageing author.

Psychological Factors

Pain is a sensory and emotional experience and thus is influenced by psychological factors. It has been suggested that anxiety lowers pain thresholds [44]. Pre-operative anxiety has been shown to be a predictor of more severe post-operative pain in studies of patients undergoing a variety of surgeries including thoracic surgery [39, 45]. Good pre-operative communication with the patient and the development of rapport will facilitate reducing the anxiety by reassurance and, if appropriate, anxiolytics [39]. A depressive mood pre-operatively [46] and neuroticism [47] have also been found to be predictors of more severe post-operative pain. There may be a relationship between pre-operative depression and the development of chronic pain [48]. Cognitive factors can also influence pain perception. Catastrophizing, a multidimensional construct with elements of rumination, magnification and helplessness, has emerged as one of the most reliable predictors of heightened pain experience [37]. Cognitive behavioural strategies may have a role in managing patients who catastrophize about pain [39].

Surgical Approach

Sternotomy

The sternum is usually internally fixed with steel wire after a sternotomy. Bone movement during respiration is thus minimal and the post-operative pain usually only moderate. However, wide or inexpert distraction of the sternum may fracture the sternum, strain or even disrupt the anterior or posterior intercostal articulations with the potential to considerably increase the post-operative pain experienced.

Video-Assisted Thoracoscopic Surgery

With video-assisted thoracoscopic (VAT) surgery the extent of the surgical incision is limited and early post-operative pain can be reduced [49]. These benefits may be reduced by the use of larger-diameter instruments and/or the twisting of surgical instruments against the ribs causing injury to the intercostal nerves and bruising or even fracturing of the ribs.

Open Thoracotomy

Posterolateral Incision

Posterolateral incision is the classic approach to a thoracotomy as it provides good surgical access and can easily be extended if required. It does, however, involve the cutting of some of the major chest wall muscles and is considered one of the most painful surgical incisions. There is some evidence that internal fixation of divided ribs reduces post-operative pain [50].

Muscle-Sparing Incision

Many surgeons now use one or more of the many muscle-sparing incisions that have been described. A popular approach is the axillary muscle-sparing incision, the skin incision for which extends vertically downwards from the axilla with obvious cosmetic advantages. Although muscle sparing incisions were initially reported to produce less peri-operative pain [51–53] most studies have not found this reduction in peri-operative pain [54, 55]. Muscle-sparing incisions may result in less chronic post-thoracotomy pain [56]. Wider rib retraction is frequently required for muscle sparing thoracotomies to compensate for the reduced field of view [55]. Wider retraction may increase the risk of rib fractures, distraction of the posterior costovertebral joints and damage to the intercostal nerves, all of which can increase post-thoracotomy pain.

Anterior Incision

Anterior incisions are used to provide access for some cardiac and anterior mediastinal procedures. Exposure for lung surgery is, however, limited particularly on the left because of the heart. Rib resections are frequently performed with this incision to improve surgical access. Post-operative pain depends in part on the extent of the excision and the extent of surgical retraction but is similar to that after a posterolateral thoracotomy. Intercostal nerve blocks are particularly effective with this approach because the incision does not involve any part of the chest supplied by the posterior cutaneous nerves which arise from the dorsal rami and are not blocked by an intercostal nerve block (see intercostal nerve blocks).

Transverse Sternothoracotomy

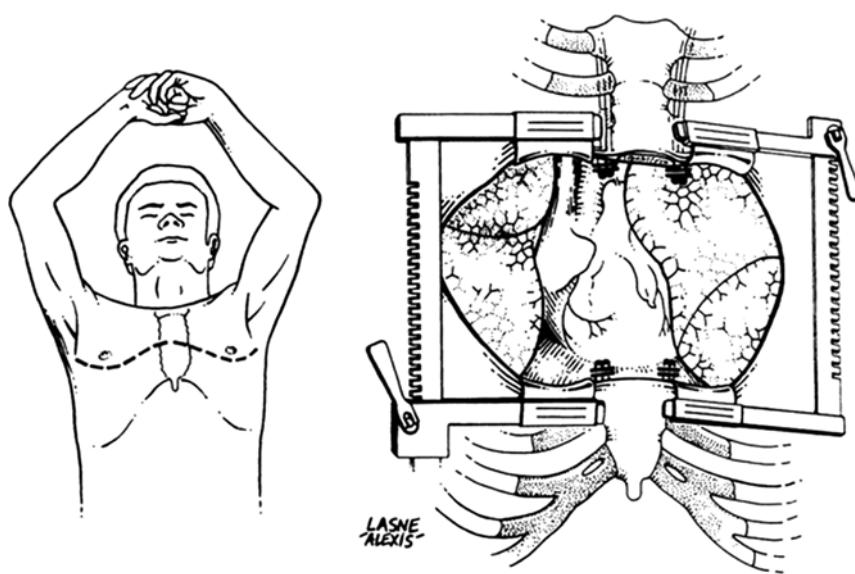
Transverse sternothoracotomy (clamshell) incisions (see Fig. 46.4) provides excellent surgical exposure of both chest cavities and the mediastinum and were in the past used for cardiac surgery. This incision results in significant post-operative pain and its use is now largely limited to lung transplantation, complex cardiopulmonary surgery and complex mediastinal tumours [57]. Post-operative pain control can be challenging with this incision.

Analgesic Drugs and Techniques

Systemic Opioids

Systemic opioids were used in the past as the mainstay of post-thoracotomy analgesia; however, the pain control achieved was often poor. It is now appreciated that for open thoracotomies systemic opioids are best administered as part of a multimodal strategy including nerve blocks. Titration of systemic opioids post-thoracotomy is needed if the balance between the beneficial effects (analgesia, enabling passive expiration,

FIG. 46.4. Schematic view of a clamshell incision (this figure was published in Macchiarini et al. [57]. © Elsevier [1999]).



prevention of splinting) and detrimental effects (sedation and suppression of ventilation, coughing and sighing) is to be achieved. In comparison to IM opioids, IV-PCA systems provide superior analgesia [58] and improve patient satisfaction [59]. In part this is because IV-PCA systems accommodate the many-fold, between patient variation, in post-operative opioid requirement [60], the halving of opioid requirements approximately every 24 h post-operatively [61] and the small group of patients that experience minimal post-surgery pain [15]. A meta-analysis published in 1998 found that compared to systemic opioids, epidural local anaesthetic significantly reduced the incidence of pulmonary complications after surgery [62]. This finding was not, however, supported by a systematic review published in 2008 [10]. Perhaps this was because of improvements in the administration of systemic opioids in later studies included in the second review. Recent studies suggest acute exposure to opioids can lead to the development of acute opioid tolerance [63].

Non-opioid Analgesic Drugs

Non-steroidal Anti-inflammatory Drugs

Prostaglandins have a role in pain perception. NSAIDs block the synthesis of prostaglandins by inhibiting the enzyme cyclooxygenase. NSAIDs reduce the inflammatory response to surgical trauma, have a peripheral non-prostaglandin analgesic effect [64] and act centrally [65] in part by inhibiting prostaglandin synthesis in the spinal cord [66]. The side effects of NSAIDs are well known and include gastrointestinal mucosal damage [67], renal tubular and platelet dysfunction [68]. The amount, if any, of NSAID mediated increased bleeding after thoracotomy has not been established, although studies after tonsillectomy suggest that the increased bleeding is probably minimal [69]. Renal failure is a particular risk for elderly patients undergoing major surgery [70, 71], patients with

pre-existing renal failure and hypovolaemic patients. These risk factors are often present in patients scheduled for thoracic surgery. There is a concern that NSAID-mediated reductions in inflammation may reduce the efficacy of a surgically performed pleurodesis. For more than 25 years, NSAIDs have been used to control post-thoracotomy pain [72]. NSAIDs have been shown to significantly improve pain control in patients receiving systemic opioids post-thoracotomy [73, 74]. NSAIDs have not been shown to significantly reduce pain scores in patients receiving thoracic epidural analgesia post-thoracotomy [75]. NSAIDs may be effective in controlling the ipsilateral shoulder pain post-thoracotomy in patients receiving thoracic epidural analgesia [18, 76], although research in this area has been limited.

COX-2 Inhibitors

Different isoenzymes of the cyclo-oxygenase enzyme exist including COX-1 and COX-2 [77]. The COX-1 isoenzyme has physiological functions while the COX-2 isoenzyme is induced during inflammation. NSAIDs vary in their selectivity for inhibiting these cyclo-oxygenase isoenzymes. Some are selective cyclo-oxygenase 2 inhibitors and are termed COX-2 inhibitors. These agents have a lower risk of causing serious upper gastrointestinal side effects and cause less platelet inhibition than the non-selective NSAIDs. There is some evidence that COX-2 inhibitors may limit the development of acute opioid tolerance [78]. There are concerns about the detrimental effects of COX-2 inhibitors (and NSAIDs) on bone growth [79, 80]. In 2004/2005, two COX-2 inhibitors (rofecoxib and valdecoxib) were withdrawn because of concerns that there was an increased risk of cardiovascular thrombotic complications when these agents were taken daily for long periods. Subsequent studies support this finding as being a COX-2 (and non-selective NSAID) class effect [81, 82]. Caution is required if these drugs are to be administered regularly.

over long periods. The safety of COX-2 inhibitors in the peri-operative setting is controversial. For patients undergoing CABG on cardiopulmonary bypass there is an increased risk of cardiovascular thrombotic events in patients receiving the selective COX-2 inhibitors parecoxib/valdecoxib [83, 84]. A study of a variety of non-cardiac surgical procedures including thoracic surgery did not show an increased incidence of cardiovascular thrombotic events in patients receiving the selective COX-2 inhibitors parecoxib/valdecoxib [85]. The level of cardiovascular risk associated with the short-term peri-operative use of COX-2 and NSAIDs remains controversial. For individual patients, their cardiovascular risk factors and the risks of alternative drugs or analgesic techniques need to be considered. The cardiovascular risk between agents varies, for example the NSAID naproxen has a lower cardiovascular risk profile than diclofenac [86].

Acetaminophen

Acetaminophen, perhaps the safest of the non-opioid analgesic agents, acts centrally by inhibiting prostaglandin synthesis [87] and possibly via the serotonergic system [88]. Acetaminophen may also have peripheral anti-inflammatory actions [89]. A recent meta-analysis found that after major surgery adding acetaminophen to morphine PCA reduced the morphine consumption by 20% but did not decrease the incidence of morphine-related adverse effects [90] (see Fig. 46.5).

There is some evidence that the effects of acetaminophen and NSAIDs are additive [91, 92]. Regular rectal acetaminophen has been shown to reduce the severity of ipsilateral post-thoracotomy shoulder pain [93]. When administered rectally the dosage should exceed the oral dose by 50%, and account should be taken of its slower onset [94]. Propacetomol, a prodrug that is hydrolysed to acetaminophen by plasma esterases, can be administered intravenously. Propacetomol has been shown to decrease morphine consumption after spinal [95] and cardiac surgery [96] although a reduction in morphine consumption after cardiac surgery was not shown in an earlier study, possibly because of the methodology [97].

Unlike NSAIDs and COX-2 inhibitors, acetaminophen at clinical doses has few contraindications or side effects. It is considered safe for patients at risk of renal failure [94]. Acetaminophen is frequently administered post-thoracotomy [3].

NMDA Antagonists

Ketamine, an anaesthetic with analgesic properties, is a non-competitive antagonist of the phencyclidine site of the NMDA receptor. Ketamine is now infrequently used for the induction or maintenance of anaesthesia because of its side effects particularly the psychomimetic effects. There is now, however, renewed interest in the use of small doses of ketamine as an adjuvant to post-operative analgesia. Activation of spinal NMDA receptors plays an important role in the development of central neuron sensitisation causing the behavioural manifestations of pain [98]. NMDA receptor antagonists enhance opioid-induced analgesia and can limit the development of opioid tolerance [98, 99]. Small doses of ketamine have been shown to have opioid sparing effects after abdominal surgery [100]. In a double-blind study of patients who had undergone thoracic surgery adding ketamine to morphine delivered via an IV-PCA system reduced morphine consumption and improved the early post-operative FEV₁ [101]. In another study, adding a low dose intravenous infusion of ketamine to thoracic epidural analgesia improved early post-thoracotomy analgesia [102]. The post-operative use of ketamine should be considered for some patients, for example patients chronically receiving high dose opioids.

Gabapentin

Gabapentin, 1-(aminomethyl)cyclohexane acetic acid, is an anticonvulsant drug that is effective in treating neuropathic pain [103] and post-herpetic neuralgia [104]. Gabapentin may act through a number of mechanisms. The most likely site of its anti-nociceptor effect is thought to be by binding to the $\alpha_2\delta$ subunit of voltage-dependent calcium channels [105]. The absorption of gabapentin is dose dependent. In the United

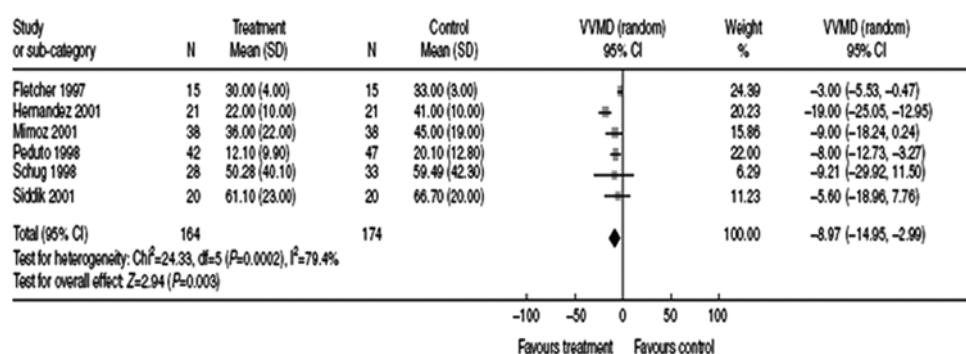


FIG. 46.5. Effect of acetaminophen on postoperative morphine consumption during the first 24 h after major surgery (reproduced from Remy et al. [90] by permission of Oxford University Press).

Kingdom, gabapentin has a product licence for the treatment of neuropathic pain. Because of its mechanism of action and effectiveness in neuropathic states its effectiveness in preventing chronic post-surgical pain has been investigated. There is as yet no clinical evidence that it reduces chronic post-surgical pain [106]. The use of gabapentin for acute peri-operative pain is “off-label”. There is good evidence that gabapentin reduces early postoperative pain scores and reduces the opioid consumption in the first 24 h for patients undergoing a variety of surgical procedures [107]. Gabapentin has been administered as a single pre-operative oral dose ranging from 300 to 1,200 mg and as multiple peri-operative doses. No additional pain reduction or opioid sparing effect was detected when multiple peri-operative doses were administered and therefore for practical purposes a single pre-operative dose of 1,200 mg or less is recommended [106]. Gabapentin is sedative and anxiolytic [108], and the doses of other premedication drugs used should be adjusted accordingly. In a placebo-controlled study, gabapentin did not decrease ipsilateral shoulder pain in patients receiving thoracic epidural analgesia [109]. Pre-operative gabapentin use should be considered in patients in whom difficulties in controlling post-thoracotomy pain are anticipated, for example patients undergoing thoracotomy in whom local anaesthetic blocks are not scheduled, and opioid tolerant patients.

Glucocorticoids

Glucocorticoids (dexamethasone) have many actions including analgesic, anti-emetic, anti-pyretic and anti-inflammatory effects. Reduced prostaglandin production by the inhibition of phospholipase and COX-2 isoenzymes is believed to be the major pathway for the analgesic effect. Dexamethasone has been shown to produce a dose-dependent opioid sparing effect [110] in a general surgical setting, and has been particularly effective in reducing pain scores with dynamic movement [111, 112]. The onset of analgesia is slower than traditional analgesics but appears to last longer and has been reported to last for up to 7 days [113]. These effects have been produced with a single dose of dexamethasone within the range of 10–40 mg with few reported serious side effects. Risks of glucocorticoid use include gastric irritation, impaired wound healing, impaired glucose homeostasis and sodium retention. The optimal dose that balances the advantages against these, and other, risks has yet to be defined and further research, particularly in the setting of thoracic surgery is required. If difficulties with post-thoracotomy pain control are anticipated and there are no contraindications to glucocorticoid use, selected patients may benefit from a single 10–16 mg dose of dexamethasone as part of a multimodal analgesia regime.

Non-pharmacologic Techniques

Transcutaneous Nerve Stimulation

Transcutaneous nerve stimulation (TENS) was developed to utilise the gate theory to reduce pain [114]. A meta-analysis published in 1996 of the effectiveness of TENS in acute

post-operative pain found little evidence for effectiveness in adequately randomised studies [115]. In contrast, TENS was considered by the original authors to be effective in most of the non-randomised studies analysed [115]. Seven studies have examined the effectiveness of adding TENS to post-thoracotomy analgesia regimens [116–122]. Some studies were not adequately randomised [117] and others inadequately blinded [116]. When appropriately analysed, most of the remaining studies did not show a significant benefit [118–120]. Although not recommended, TENS may possibly be of some benefit after VAT surgery [120].

Cryoanalgesia

While the chest is open the intercostal nerves can be blocked for up to 6 months by the application of a cryoprobe. The analgesia is inferior to thoracic epidural fentanyl [123] and the technique is associated with an increased incidence of chronic post-thoracotomy pain [124]. Cryoanalgesia is now rarely used to provide post-thoracotomy analgesia and cannot be recommended.

Specific Techniques

Continuous Wound Infiltration Catheters

Randomised studies have shown that delivering local anaesthetic into the wound via catheters placed prior to closure can reduce post-operative opioid use [125] and may reduce wound oedema [126]. For patients receiving continuous paravertebral infusions, the potential for local anaesthetic toxicity usually makes this technique inappropriate. For patients receiving thoracic epidural analgesia, this technique is usually unnecessary. It should, however, be considered for patients not scheduled to receive local anaesthetic infusions by other routes for post-operative pain control.

Intercostal Nerve Blocks

The spinal nerves divide into a dorsal and ventral ramus. The upper eleven thoracic ventral rami form the intercostal nerve which runs forward between the ribs in the intercostal spaces. Each intercostal nerve gives off a lateral cutaneous branch that pierces the intercostal muscles proximal to the posterior axillary line to supply the lateral aspect of the chest wall. It is important therefore the intercostal nerves are blocked proximal to the posterior axillary line to ensure that the lateral cutaneous branches and thus the lateral aspect of the chest wall are blocked. The thoracic dorsal rami pass backwards close to the vertebrae to supply the cutaneous innervation to the back. The dorsal rami are not blocked by an intercostal nerve block. This limits the effectiveness of intercostal nerve blocks for posterolateral thoracotomies (see Fig. 46.6).

The intercostal nerves can easily be blocked under direct vision while the chest is open but because of the relatively

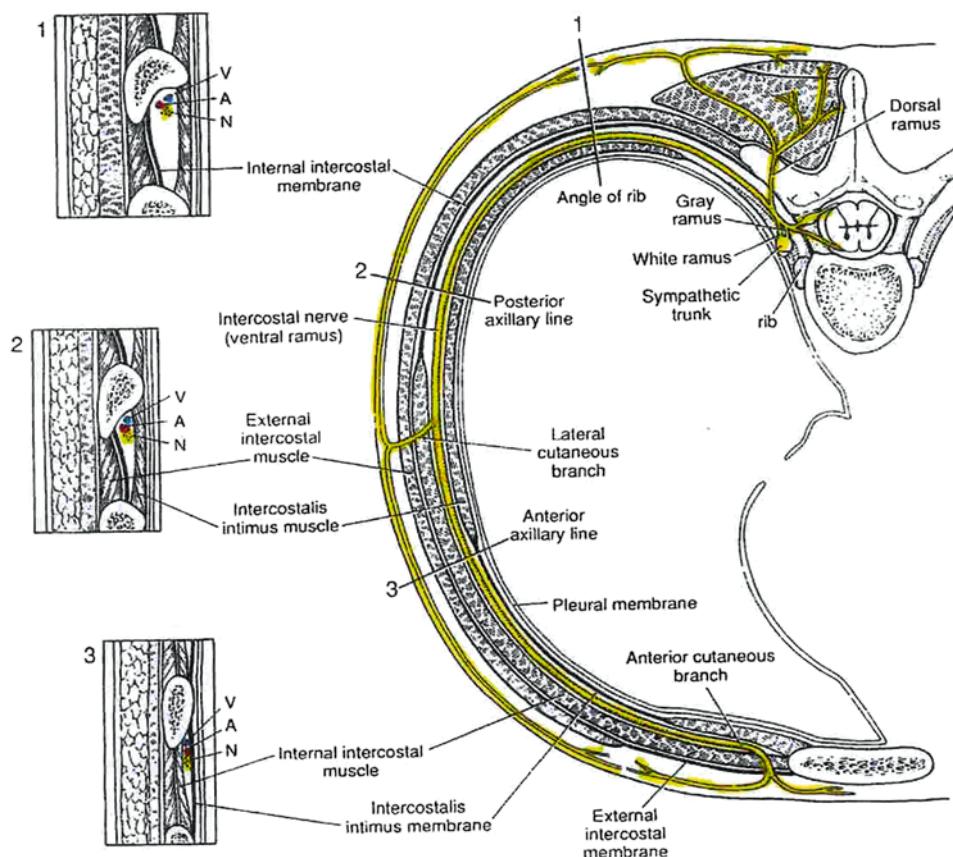


FIG. 46.6. Anatomy of intercostal nerve and space (reproduced with permission from Dravid and Paul [131]. © Blackwell Publishing Limited [2007]).

short half-life of most local anaesthetics repeated percutaneous blocks are usually required. The intercostal nerves consistently lie in a plane deep to the internal intercostal muscle although there is considerable variability in the position of intercostal nerves within the intercostal spaces [127]. Small (5 mL) bolus of local anaesthetic deposited in the correct plane will block the appropriate intercostal nerve. Larger doses may also block adjacent intercostal nerves by spreading medially to the paravertebral space or directly to the adjacent spaces (see Fig. 46.7). The systemic uptake of local anaesthetic from the highly vascular intercostal space is rapid and the dose of local anaesthetic administered by this route needs to be appropriately limited. Intercostal nerve blocks significantly reduce post-operative pain and analgesic requirements post-thoracotomy [128–130].

Interpleural Blocks

In healthy human adults, the two layers of the pleura have a surface area of about 0.2 m^2 , are separated by a distance of 10–20 μm and contain approximately 10 mL of pleural fluid [131]. The deposition of local anaesthetic between the parietal and visceral pleura with the aim of producing an ipsilateral somatic block of multiple thoracic dermatomes constitutes an interpleural block and was originally described by Kvalheim

and Reiestad [132]. Unfortunately, the terminology used in the literature to describe this block can be confusing, some authors use the term intrapleural block [133] and others pleural block [134]. The issue is further confused when the term interpleural block is used to describe a paravertebral block [135]. Although studies have consistently shown interpleural blocks to be effective for pain relief after cholecystectomy [135] most studies of patients undergoing a thoracotomy have shown interpleural blocks to be ineffective [136–139]. The wide spread of local anaesthetic within the normally small (10 mL) pleural space is aided by surface tension forces and this probably accounts for the effectiveness of interpleural blocks after cholecystectomy. After thoracotomy the volume of the pleural space is much larger and contains blood and air. The effect of surface tension forces is reduced and the spread of local anaesthetics is limited and principally via gravity. Dilution of the administered local anaesthetic by interpleural blood [140] and the loss of local anaesthetic into the chest drains [139–141] further reduce the efficacy of this technique. A possible role for interpleural bupivacaine, administered post-thoracotomy via the basal chest drain, to reduce local diaphragmatic irritation from the basal chest drain was explored in a double-blind study. Interpleural local anaesthetic administered by this route was found to be ineffective [142]. Systemic absorption of interpleurally administered local anaesthetic can be considerable and high

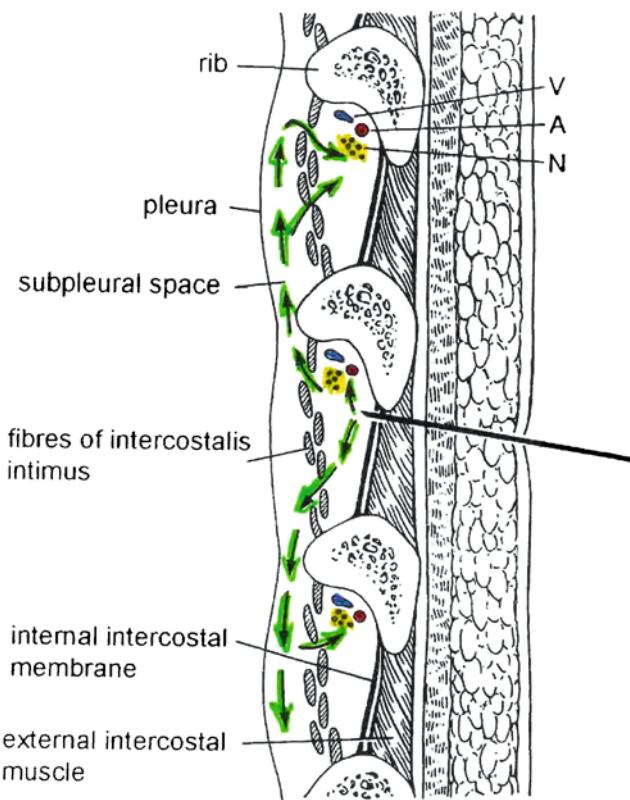


FIG. 46.7. Intercostal nerve block. Showing spread of local anaesthetic to adjacent spaces (arrows) (reproduced with permission from David and Paul [131]. © Blackwell Publishing Limited [2007]).

plasma levels of local anaesthetics have been reported [138]. Interpleural blocks are not recommended for post-thoracotomy analgesia in adults [10].

Paravertebral Blocks

Paravertebral blocks were introduced into clinical practice in 1906 [143] and were then largely abandoned before being reintroduced in 1979 [144]. There has now been substantial experience in the use of thoracic paravertebral block for thoracic surgery and their safety has been established. Continuous thoracic paravertebral blocks can provide excellent post-thoracotomy analgesia and a number of studies have shown that the analgesia is comparable to that provided by thoracic epidurals but with fewer complications [11]. Not all clinicians, however, are able to get reliably good analgesia with paravertebral blocks. Paravertebral block failures may occur for a number of reasons including failure to place or maintain the catheter in the paravertebral space, failure to contain the local anaesthetic solution within the paravertebral space and failure to deposit local anaesthetic at the appropriate level or extend the block over sufficient dermatomes to provide adequate analgesia. Although it is possible to blindly place catheters percutaneously into the paravertebral space it

is often more appropriate for the surgeon to insert the catheter into the paravertebral space under direct vision while the chest is open. Direct placement facilitates advancement of the catheter along the paravertebral space to create a narrow longitudinal pocket that will block sufficient dermatomes to provide adequate analgesia.

Anatomy

The paravertebral space is a potential space. At the thoracic level the paravertebral space is a wedge-shaped area bounded posteriorly by the costo-transverse ligaments, transverse processes and necks of the ribs (see Fig. 46.8). Medially it is bound by the vertebral bodies, discs and intervertebral foramina. The anterior border of the space is formed by the parietal pleura. Lateral to the tips of the transverse processes the paravertebral space is continuous with the intercostal neurovascular space (see Fig. 46.9).

The paravertebral space is contiguous with the paravertebral spaces above and below. The caudal boundary is formed by the psoas major muscle [145], the cranial boundary is, however, not well defined [146]. The thoracic paravertebral space is divided into an anterior subpleural paravertebral compartment and a posterior subendothoracic paravertebral compartment by the endothoracic fascia which is the deep fascia of the thorax [146] (see Fig. 46.10). Contained within the paravertebral space are the dorsal and ventral rami of the spinal nerves, the grey and white rami communicans and the sympathetic chain. The intercostal nerves (ventral ramus) are devoid of a fascial sheath within the paravertebral space making them highly susceptible to local anaesthetic block at this site [147].

Methods of Performing Paravertebral Blocks

The relatively short duration action of clinically available local anaesthetics makes single bolus paravertebral blocks inappropriate for most post-thoracotomy patients. Paravertebral blocks are best established with a bolus of local anaesthetic and maintained with a constant infusion of local anaesthetic via a catheter placed in the paravertebral space. Ultra long-acting local anaesthetic agents are being developed and placement of these agents in the paravertebral space may in the future make single bolus paravertebral blocks practical and thereby reduce the risks of local anaesthetic toxicity and block failure because of catheter displacement. Biodegradable bupivacaine-containing polymer microcapsules can produce prolonged local anaesthesia [148], adding a glucocorticoid prolongs the effect further [149]. In sheep the granulomatous reactions that occurred around the bupivacaine microcapsules can be prevented by adding dexamethasone [150]. Bupivacaine–dexamethasone microcapsules have been shown to produce an intercostal nerve block of up to 4 days duration in humans [151]. Bupivacaine has also

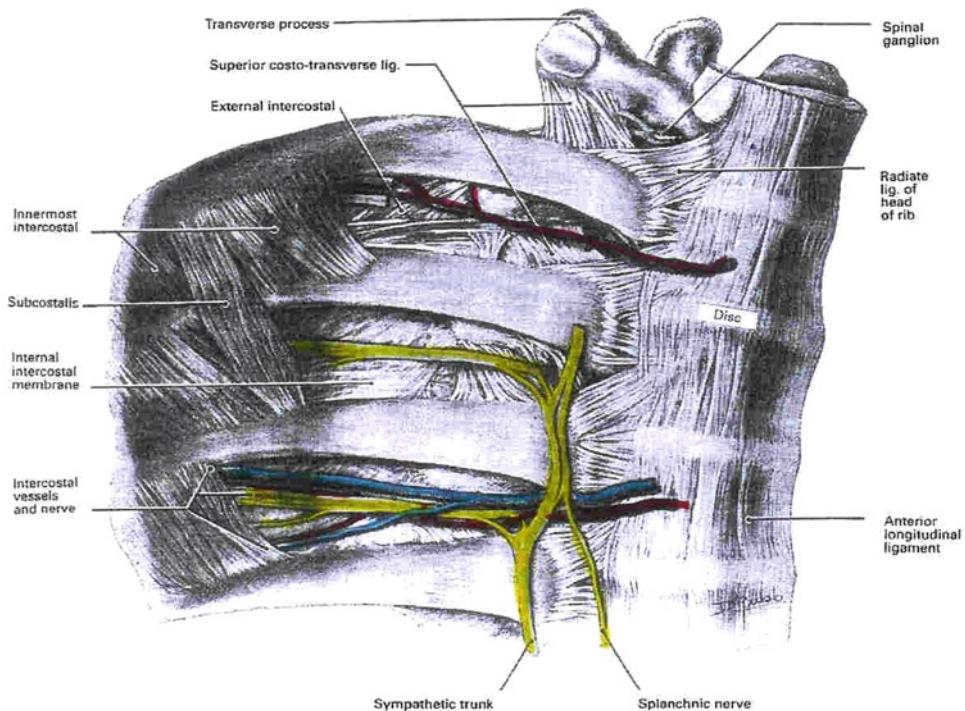


FIG. 46.8. Posterior relations of the thoracic paravertebral space (reproduced from Murphy [135] by permission of Oxford University Press).

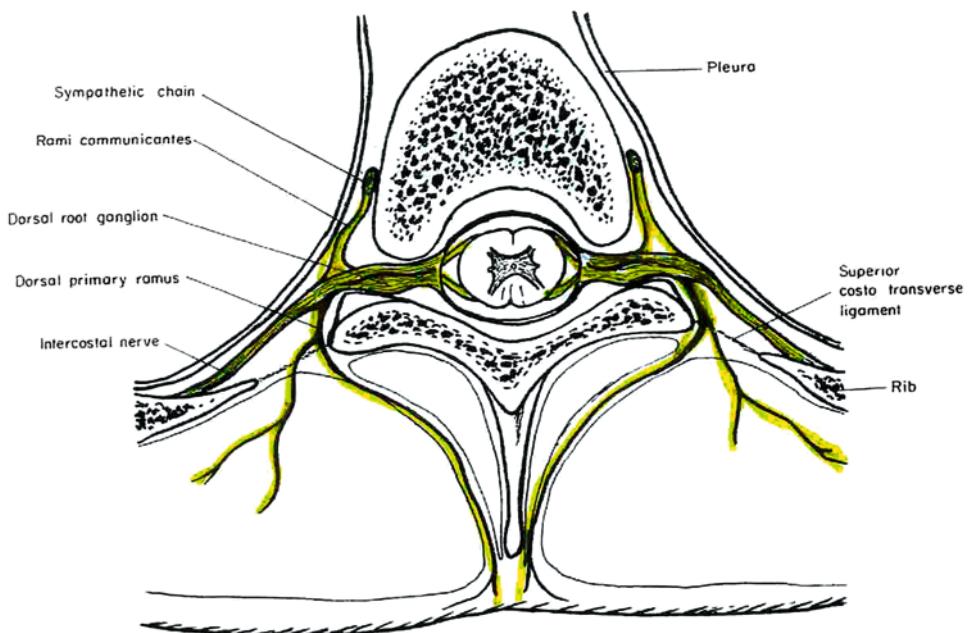


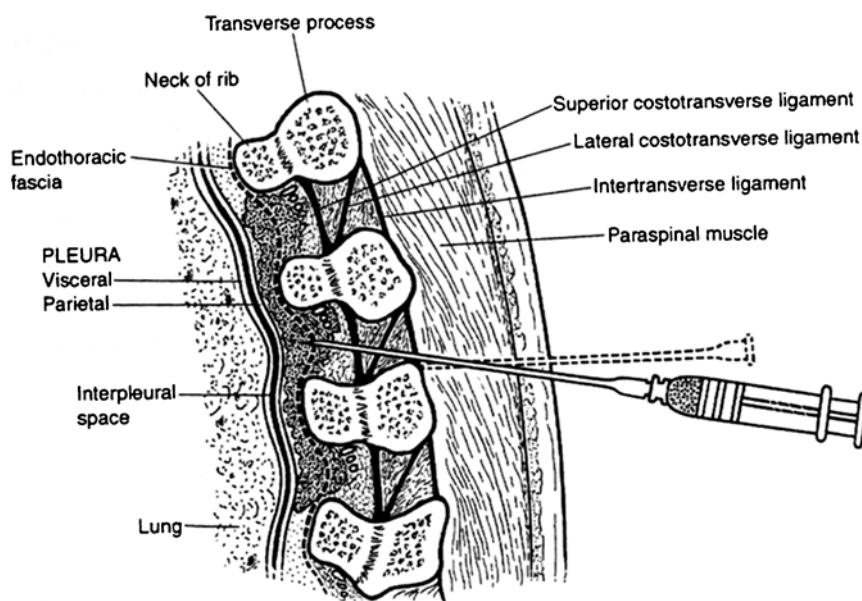
FIG. 46.9. Transverse section at the level of the intervertebral foramen showing the paravertebral spaces (reproduced with permission from Eason and Wyatt [144]. © Blackwell Publishing Limited [1979]).

been incorporated into liposomes [152]. Liposomal bupivacaine has a prolonged action in animals [153] and has been used to provide post-operative epidural analgesia in humans [154]. Recently, an absorbable local anaesthetic matrix has been used in rats [155].

Percutaneous Methods

A number of different techniques for the percutaneous placement of paravertebral catheters have been described. Perhaps the most widely used technique is the one described

FIG. 46.10. Saggital section through the paravertebral space showing a needle that has been walked off the transverse process (reproduced from Karmakar [146] with permission).



by Eason and Wyatt [144]. For the Eason technique, a Tuohy needle is inserted 3 cm lateral to the cranial edge of a spinous process at the appropriate level. The needle is then advanced perpendicular to the skin until contact is made with the underlying transverse process. If contact with bone is not made at the expected depth the needle is withdrawn and then re-advanced slowly, while fanning it in the sagittal plane, until contact with bone is made. The needle is then walked off the cranial edge of the transverse process and advanced slowly until a loss of resistance, less complete than that in the epidural space, is encountered, usually after a further 1 cm. This is frequently preceded by a subtle click as the costotransverse ligament is penetrated. In adults after aspiration, to confirm the needle is extravascular, approximately 20 mL of an appropriate local anaesthetic (e.g. 0.25% levobupivacaine) is administered to open up the paravertebral space before threading an epidural catheter into the paravertebral space. Consideration may be given to adding a small quantity of dye to the local anaesthetic administered, so correct placement of the block can be confirmed visually at subsequent thoracoscopy or thoracotomy.

An alternative technique whereby the paravertebral space is approached from an intercostal space has recently been described [156]. A Tuohy needle is positioned posteriorly over a rib at the appropriate level about 8 cm lateral to the head of that rib and advanced until contact is made with the rib. The needle is then orientated so the bevel is pointing medially and the tip is angulated 45° cephalad and 60° medial to the sagittal plane. The needle tip is then walked off the inferior border of the rib while maintaining this orientation and advanced a few millimetres until loss of resistance confirms that the intercostal neurovascular space has been entered. After aspirating to confirm the needle is extravascular approximately 5 mL of 0.25% levobupivacaine is injected to open up the intercostal neurovascular space. An epidural catheter is then inserted into the

Tuohy needle and advanced into the intercostal neurovascular space. The orientation of the needle directs the catheter along the intercostal neurovascular space towards the paravertebral space. The catheter is inserted about 8 cm into the intercostals space so the tip lies in the paravertebral space [156]. Percutaneous thoracic paravertebral blocks are technically simple to perform but have a failure rate of up to 10%. The use of ultrasound guidance may result in reduced failure rates. Failure rates can also be reduced by direct surgical placement.

Open Methods

Direct placement techniques may require some surgical pre-planning. The posterior extent of the incision needs to be limited to allow sufficient room for the paravertebral. In particular it is important to preserve enough pleura posterior to the surgical incision. Direct placement techniques are usually undertaken at the end of surgery immediately prior to closure to reduce the risk of inadvertent catheter dislodgement. The direct placement of catheter into the paravertebral space at the end of surgery was first popularised by Sabanathan et al. [157]. They described a technique whereby a catheter is inserted via a Tuohy needle. The catheter is inserted percutaneously medial to the posterior edge of the thoracotomy incision to emerge between the angle of the ribs into the chest cavity. The parietal pleura two spaces above and below the incision is peeled back medially to expose the intercostal nerves taking care not to perforate the pleura. The catheter is then positioned to lie against the angles of the exposed ribs before the parietal pleura is reattached to the posterior aspect of the wound. The authors later reported an improvement in their technique [158]. After reflecting back the parietal pleura to the vertebral bodies as before, a small incision is made in the endothoracic fascia and the catheter is passed into the subendothoracic paravertebral

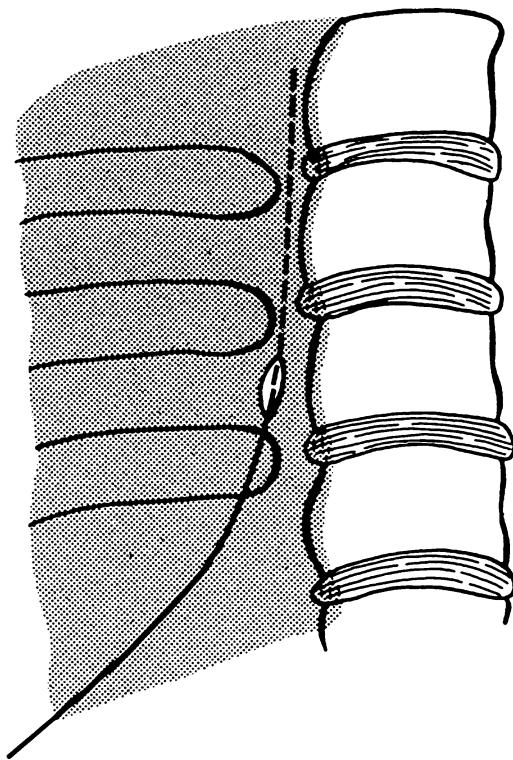


FIG. 46.11. A technique for performing paravertebral blocks. The endothoracic fascia (stippled) is exposed by raising the parietal pleura from the posterior chest wall. A catheter is inserted deep to the endothoracic fascia through a small hole created in the fascia (this figure was published Berrisford and Sabanathan [158]. © Elsevier [1990]).

compartment and advanced cranially for a few centimetres, aided if necessary by blunt dissection. The hole in the endothoracic fascia is then closed by a suture (see Fig. 46.11).

Another technique used in the author's institution is for the surgeon to insert a Tuohy needle percutaneous, under direct vision, into the paravertebral space one or two segments caudal to the thoracotomy incision. A catheter is then introduced through the Tuohy needle and advanced 10 cm or more cranially in the paravertebral space. This requires careful manipulation of the Tuohy needle and catheter to ensure it advances in the correct direction and damage to the overlying pleura is avoided. The other end of the catheter can then be tunneled subcutaneously to limit the risk of inadvertent dislodgement. For patients undergoing video-assisted surgery, video-assisted surgical placement of a catheter is possible [159].

Management of Paravertebrals

The appropriate management of paravertebrals (drug choice, rate, adjuvant and administration technique) has not yet been established and further work is required to optimise the efficacy and safety of this technique. A review and meta-regression analysis [160] found that a higher bupivacaine

dose (890–990 mg per 24 h) predicted lower pain scores and faster recovery of pulmonary function compared to lower dose (325–472.5 mg) without a significant difference in the rate of local anaesthetic toxicity. Continuous infusions were associated with significantly lower pain scores than intermittent boluses while the addition of adjuvants, fentanyl or clonidine, did not improve the analgesia. The use of safer local anaesthetic, such as levobupivacaine, vigilance for signs and symptoms of local toxicity (confusion), the addition of adrenaline to the solution and reducing the infusion rate for elderly or frail patients may all be appropriate steps to reduce the incidence of toxicity with the use of paravertebrals. A typical dosing regime for an adult patient might be 0.3 mL kg^{-1} initial bolus of 0.25% levobupivacaine followed by a $0.1 \text{ mL kg}^{-1} \text{ h}^{-1}$ infusion of 0.25% levobupivacaine (see Table 46.2).

Limitations and Complications of Paravertebral Blocks

To provide effective analgesia in the affected somatic dermatomes, post-thoracotomy paravertebral blocks may need to cover up to ten segments. It usually takes a number of hours for the local anaesthetic to spread sufficiently along the paravertebral space and as a result the early post-operative analgesia may be poor unless supplemented initially by other analgesic agents or techniques. Complications that have been reported include inadvertent pleural puncture, pulmonary haemorrhage, inadvertent dural puncture, hypotension, nerve injury and central nervous system local anaesthetic toxicity. The incidence of these complications is low but the available published data does not enable an exact incidence to be quoted to patients [146]. Many of the potential complications of paravertebrals can be greatly reduced, if not eliminated, by using an open method of insertion. However, the large volume of local anaesthetic required and rapid uptake of local anaesthesia from the vessel-rich paravertebral space mean that local anaesthetic toxicity is a concern. Mean plasma concentrations have been shown to exceed the threshold for central nervous system toxicity 48 h after commencing a $0.1 \text{ mL kg}^{-1} \text{ h}^{-1}$ infusion of 0.5% bupivacaine [161]. In a separate study of patients receiving paravertebral 0.5% bupivacaine at this rate, 7% of patients developed temporary confusion attributed to bupivacaine accumulation [162]. Until recently, there has been no specific treatment available for local anaesthetic toxicity. There is now a growing body of evidence from animal studies and case reports that lipid emulsion given intravenously improves outcome. It is therefore recommended that lipid emulsion is available wherever patients receive large doses of local anaesthetic such as for a paravertebral block. The management of local anaesthetic toxicity induced cardiovascular collapse should involve CPR as per standard protocols followed by the consideration to administer a lipid emulsion [163, 164]. To put the risks in perspective, no fatality directly related to thoracic paravertebral block had been reported by 2001 [146].

TABLE 46.2. Adult analgesic regimes.

Technique	Dose	Comment
<i>Paravertebrals</i>		
Lower dose regime		
Loading dose	0.3 mL kg ⁻¹ 0.25% Levobupivacaine	
Maintenance	0.1 mL kg ⁻¹ h ⁻¹ 0.25% Levobupivacaine	Higher dose regime produces improved analgesia and pulmonary function [160]
High dose regime		
Loading dose	20 mL 0.5% Levobupivacaine	
Maintenance	0.1 mL kg ⁻¹ h ⁻¹ 0.5% Levobupivacaine	
<i>Intrathecal opioids</i>		
	Morphine 200 µg + sufentanil 20 µg [166] or morphine 500 µg + sufentanil 50 µg [167]	
<i>Thoracic epidural</i>		
Levobupivacaine or	0.1%	Titrate to effect
Ropivacaine with	0.15%	Reduce rate by 40% for elderly
Fentanyl	4–5 µg mL ⁻¹ or	
Sufentanil	1 µg mL ⁻¹ or	
Hydromorphone	10–25 µg mL ⁻¹ [280]	
Bolus	7 mL	
Infusion	7 mL h ⁻¹	
<i>Intercostal nerve blocks</i>		
Injection sites T3–T7	0.25% Levobupivacaine with epinephrine 1:200,000 3–5 mL per site	Use repeated doses or continuous infusion [10]. Associated with rapid absorption of local anaesthetic
<i>Ketamine</i>		
For intravenous supplementation of epidural analgesia	0.05 mg kg ⁻¹ h ⁻¹ [102]	
Without epidural analgesia		
Bolus	0.5 mg kg ⁻¹ [274]	
Infusion	4 µg kg ⁻¹ min ⁻¹ Continued for few days [274]	
<i>Gabapentin</i>	300–1,200 mg Orally 1–2 h pre-operatively [106]	No benefit from multiple post operative doses [106]

Advantages of Paravertebral Analgesia

Paravertebral block is a relatively simple technique that is easy to learn, has few contraindications and has a low incidence of complications. The open technique enables paravertebral blocks to be safely initiated in anaesthetised patients. This makes the technique particularly appropriate for patients in whom a VAT procedure is converted to an open thoracotomy. Impaired coagulation is a relative contraindication to the percutaneous insertion of paravertebrals. However, for patients with impaired coagulation open placement is relatively safe and can be recommended. Hypotension, urinary retention, nausea and vomiting are less frequent post-operatively with paravertebrals than with thoracic epidurals [11]. In the author's institution, paravertebrals are associated with earlier mobilisation and shorter hospital stays than thoracic epidurals.

Intrathecal Analgesia

The lumbar administration of subarachnoid opioids is an infrequently used technique that may have a wider role in

providing post-thoracotomy analgesia. The use of intrathecal morphine to provide operative analgesia was first described in 1979 [165]. Since then a number of studies have reported the use of intrathecal opioids for post-thoracotomy analgesia [166–172]. The onset time of intrathecal opioids depends in part on their lipid solubility [173]. With intrathecal sufentanil the onset of analgesia is very rapid whereas morphine has a slower onset but longer duration of action. Combinations of morphine and sufentanil have been used to provide post-thoracotomy analgesia. In one study, morphine 200 µg was combined with sufentanil 20 µg [166] in another study morphine 500 µg was combined with sufentanil 50 µg [167] both studies reported good early analgesia. Side effects of intrathecal opioids include nausea, vomiting, pruritus, urinary retention and delayed respiratory depression. The lumbar epidural space is easy to locate making it an attractive technique in patients with, for example fixed spinal deformities. The combination of low-dose intrathecal morphine and a paravertebral block via a directly placed catheter has been suggested as an alternative to epidural analgesia post-thoracotomy [174].

Epidural Analgesia

Epidural injections via the sacral hiatus in dogs were described in 1901 [175]. The interspinous approach for epidural anaesthesia in clinical surgery was demonstrated in 1921 [176] and an article in 1933 by Dogliotti popularised epidural anaesthesia [177].

Post-thoracotomy thoracic epidural analgesia was introduced into clinical practice in the mid-1970s for high risk procedures [1, 2], by the mid-1980s it was being used by some for routine surgery [178] and by the 1990s it had become the mainstay of post-thoracotomy analgesia in many high volume Western units [3]. The widespread use of thoracic epidural for routine post-thoracotomy analgesia occurred because it provides effective, reliable post-thoracotomy analgesia, had been shown in a meta-analysis to reduce post-thoracotomy pulmonary complication [62] and was believed by many to improve the outcome after thoracic surgery.

Lumbar Epidural Analgesia

Lumbar epidural insertion is an easier and more familiar technique for most anaesthesiologists and also because of the absence of an underlying spinal cord lumbar epidurals are probably safer than thoracic epidurals. Lumbar epidural hydrophilic opioids are effective and were once used by a number of units to provide post-thoracotomy analgesia. Their widespread use declined when a meta-analysis showed that, unlike epidural local anaesthetics, epidural opioids did not reduce the incidence of post-operative pulmonary complications [62]. Late respiratory depression is also a potential problem with epidural hydrophilic opioids. Because of synergistic antinociceptive interactions, mixtures of local anaesthetics and opioids are now routinely used to provide post-thoracotomy analgesia [14]. Epidural mixtures of segmentally acting lipophilic opioids and local anaesthetics are best administered at the dermatomal level of the surgical incision. For thoracic procedures, this equates to a thoracic epidural. If the mixture is administered by a lumbar epidural away from the incision larger volumes are required, greater hemodynamic instability results and achieving good analgesia is more difficult. Lumbar epidurals are not now generally used for providing post-thoracotomy analgesia; however, in the occasional patient in whom attempts at placing a thoracic epidural are unsuccessful, a lumbar epidural may be appropriate. It is also a technique worth considering in the rare circumstance in which it is considered appropriate to insert an epidural in an anaesthetised patient.

Thoracic Epidural Analgesia

Technique of Insertion

After inserting a venous cannula and positioning the patient in either the lateral or sitting position, depending largely on operator preference, a wide area of the back is prepped with alcoholic chlorhexidine or an alternative antiseptic solution.

At least two applications are recommended. The initial application should be with a sponge or similar material to abrade the superficial layers of the skin. Care should be taken to ensure that epidural drugs and equipment are not contaminated by the antiseptic used as all antiseptics are potentially neurotoxic. Similarly, the antiseptic solution used should be allowed to dry before commencing epidural insertion. The vertebral spinous processes are at their most oblique in the midthoracic region. At this level the tip of the spinous process is a landmark for the intervertebral space below the next vertebrae (see Fig. 46.12).

For the midline approach, a local anaesthetic wheal is raised over the appropriate vertebral interspace. A Tuohy needle is then inserted immediately above the palpable tip of the lower spinous process and advanced at the oblique cephalad angle determined by the obliquity of the spinous processes at this particular level. The angle of insertion may need adjustment if contact is made with a spinous process. For the paramedian approach, a local anaesthetic wheal is raised about 1 cm lateral to the palpable tip of the appropriate spinous process. A Tuohy needle is then inserted through this wheal perpendicular to all the planes. When contact is made with bone (lamina) the needle is withdrawn to the skin and angulated about 45° cephalad and 10° medial before being reinserted to the original depth¹.



FIG. 46.12. The thoracic vertebra. The steepest caudal inclination of the spinous processes is in the midthoracic region (this figure was published in Ramamurthy [277]. © Elsevier [1996]).

¹Editors note: It has been my personal experience that the paramedian approach has greatly improved my success rate for mid-thoracic epidurals, T3–T8, deliberately walking the Tuohy needle medially and up the lamina.

The needle is then gradually advanced into the epidural space. If contact is again made with the lamina it may be necessary to walk the needle up the lamina to find the epidural space. After the tip of the Touhy needle has been in contact with bone it is advisable to ensure that the needle remains patent by gently re-inserting the trocar before re-advancing the needle.

It is known that during insertion epidural catheters do not follow a predictable course in the epidural space [179]. The optimal length of epidural catheter to leave in the epidural space is thus a balance between insufficient length resulting in catheter migration out of the space and excessive length resulting in technical failure because of malpositioning of the catheter tip. In a prospective analysis of post-operative epidural failure by computed tomography epidurography during which 4 cm of epidural catheter was left in the epidural space 25% of the epidurals failed. The major cause of epidural failure was dislodgement of the epidural catheter out of the epidural space [180]. Four centimetre of catheter is probably insufficient for thoracic epidurals that are to remain in situ for a few days, 5–6 cm may be more appropriate [181]. Migration of the catheter out of the epidural space can be reduced by appropriate fixation with adhesive dressings, tunnelling or suturing. We recommend suturing of the catheter to the skin.

Epidural Solutions

High concentrations of unsupplemented thoracic epidural local anaesthetics can provide effective post-thoracotomy analgesia but the incidence of hypotension is high [182], while lower concentrations are less effective. Because the synergistic antinociceptive interactions of epidural local anaesthetics and opioids [183] enable the amount of each drug to be minimised reducing the incidence and severity of the associated side effects, mixtures of local anaesthetics and opioids are now routinely used to provide post-thoracotomy analgesia [14]. Although there is probably no epidural mixture that is optimal for all patients, a mixture of 5 $\mu\text{g mL}^{-1}$ of fentanyl in 0.1% bupivacaine is close to the optimal [184–186]. The newer local anaesthetic agents (levobupivacaine and ropivacaine) are less toxic than bupivacaine and although relatively small amounts are administered epidurally, we now use 5 $\mu\text{g mL}^{-1}$ of fentanyl in 0.1% levobupivacaine. The analgesic effects of epidural opioid and local anaesthetic mixtures are improved by epinephrine. Vasoconstriction of epidural vessels with reduced systemic uptake of epidural opioids is thought to be the major cause of this potentiation. The α -2 adrenergic action of epinephrine in the substantia gelatinosa may also contribute to the improved analgesia [187]. Potential cord ischaemia as a result of excessive vasoconstrictive has limited the use of epidural epinephrine. Clonidine, another α -2 adrenergic agonist, when combined with epidural opioids, reduces opioid requirements and opioid-related side effects [188]. In a study using an optimisation model to find the best epidural combination of fentanyl, bupivacaine and clonidine to administer after laparotomy, the addition of clonidine did not significantly improve

analgesia [184]. Epidural clonidine is not widely used to provide post-thoracotomy analgesia [14], although the addition of clonidine should be considered for patients who are particularly sensitive to the systemic effects of epidural opioids.

The extent of the sensory block after the administration of epidural anaesthetics varies considerably between individuals. A number of factors are known to affect the spread of the sensory block during thoracic epidural analgesia including the level at which the epidural is sited. For high thoracic epidurals the direction of spread is mainly caudal, for low thoracic epidurals the spread is mainly cranial and for midthoracic epidurals the spread is almost equally distributed [41, 189]. The total extent of the spread, however, is not significantly different at these three sites [41, 189]. While administering an epidural solution via a high thoracic epidural it may be appropriate to avoid neck flexion to further limit the potentially harmful cranial spread of the epidural solution [190]. Although widely believed and apparently logical, there is little evidence that the extent of thoracic epidural spread is related to the height of the patient [41]. Similarly, for adult patients weight does not appear to correlate with the extent of thoracic epidural spread [41]. There is, however, a positive correlation between the patient's age and the thoracic epidural spread, with elderly patients requiring about 40% less epidural solution [41, 42]. For younger patients, we usually administer a ~7 mL epidural bolus of a mixture containing 5 $\mu\text{g mL}^{-1}$ of fentanyl in 0.1% levobupivacaine via a midthoracic catheter and then infuse the epidural solution at ~7 mL h⁻¹. For elderly patients, we reduce the bolus and infusion rate by about 40% (see Table 46.2 and Fig. 46.13)².

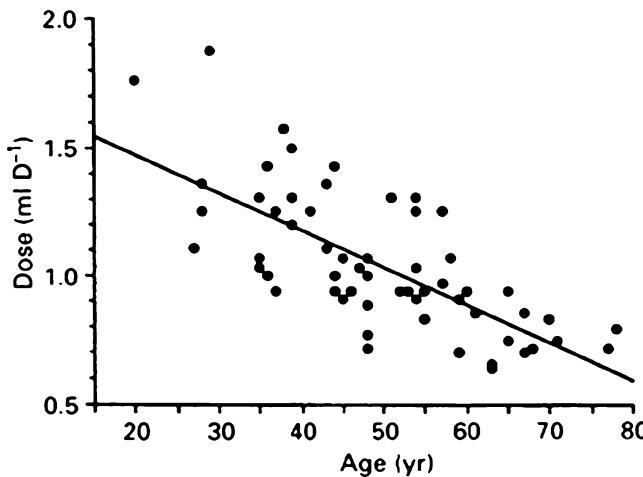


FIG. 46.13. Relationship between age and epidural dose requirements of 2% mepivacaine in thoracic epidural analgesia. D Dermatome (reproduced from Hirabayashi and Shimizu [42] by permission of Oxford University Press).

²Editors note: Several alternative protocols for thoracic epidural infusions are described in the addendum at the end of this chapter.

Benefits of Thoracic Epidural Analgesia

Thoracic epidurals provide excellent early post-thoracotomy analgesia and are widely regarded as the “gold standard” for post-thoracotomy pain relief.

Improved Post-operative Diaphragmatic Dysfunction

Prolonged diaphragmatic dysfunction has been shown to occur after thoracic [191] and upper abdominal [192] surgery. Diaphragmatic contractility is not impaired [193, 194] and the diaphragmatic dysfunction is thought to be secondary to reflex inhibition of the phrenic nerve as a result of stimulation of afferents in the viscera, diaphragm and chest wall [193]. Pain is not considered to be a major mediator of this dysfunction [195]. Thoracic epidural local anaesthetics have been shown to improve diaphragmatic function after upper abdominal surgery [196]. Epidural opioids are not effective [192]. Thoracic epidural local anaesthetics have not been shown to improve the impaired diaphragmatic segmental shortening after thoracotomy but other ventilatory parameters did improve. However, as epidural local anaesthetics can alter other respiratory muscle functions the improvement in diaphragmatic function may have been masked [191]. Thoracic epidural analgesia may directly affect functional residual capacity post-thoracotomy as an increase in functional residual capacity occurs in healthy humans receiving thoracic epidural analgesia [197].

Reduced Cardiovascular Complications

Cardiovascular complications contribute significantly to post-thoracotomy morbidity and mortality. Thoracic epidural local anaesthetics can block the sympathetic nerve fibres to the heart (T1–T5) and have been used to treat refractory angina [198, 199]. Thoracic epidural analgesia can also dilate constricted coronary arteries and improve the hemodynamic stability of patients undergoing thoracic surgery. These changes have the potential to reduce myocardial ischaemia. A meta-analysis of patients undergoing various surgeries has confirmed this potential and shows that epidural analgesia reduces post-operative myocardial infarctions by 40%; thoracic epidural analgesia is superior to lumbar epidural analgesia in this respect [200]. There is some evidence that thoracic epidural local anaesthetics reduce the incidence of supraventricular arrhythmias [201], which occur in 20–30% of post-thoracotomy patients [202, 203] and are associated with an increased mortality [204, 205].

Thoracic Epidurals and Outcome

The mortality from lung cancer surgery has decreased over the last few decades and this reduction in post-thoracotomy mortality has been attributed, in part, to improvements in post-operative analgesia. There are a number of possible mechanisms whereby thoracic epidural analgesia may reduce respiratory complications post-thoracotomy. These include better preservation of functional residual capacity, improved mucociliary clearance, reduction of inhibitory effects on the diaphragm, less pain, nausea and sedation and better collaboration with physiotherapy.

Although transferable evidence and early analysis found that when compared with systemic analgesia, thoracic epidural analgesia reduced post-operative pulmonary complications [62], later quantitative analyses have not shown this reduction [10]. Similarly, although thoracic epidurals may decrease peri-operative myocardial infarctions [200] and reduce the incidence of thrombo-embolic events [206, 207] there are no prospective studies showing thoracic epidurals improve survival after thoracotomy. A meta-analysis of randomised controlled studies did show reduced mortality with neuroaxial blocks after surgery but much of this effect was after orthopaedic surgery [208]. In contrast, a large prospective randomised study of patients undergoing major abdominal surgery did not show epidural analgesia to be associated with reduced mortality [209]. A large prospective study is required to determine if post-thoracotomy outcome is improved with thoracic epidural analgesia.

Limitations and Adverse Effects

The reported rates of epidural failure vary. Although successful catheter placement rates of 99% and subsequent technical failure rates of <1% have been reported [210], some audits have reported a 30–50% failure rate [211] and a recent meta-analysis reported a 15% thoracic epidural failure rate [11]. Thoracic epidurals are considered technically more difficult to insert than lumbar epidurals; however, the dural perforation rate has been found to be lower during thoracic epidural insertion (0.9%) than during lumbar epidural insertion (3.4%) [210]. Respiratory depression is a concern with epidural opioids particularly hydrophilic opioids. The incidence is related to the type and dose of the epidural opioids used. A Swedish study also found that age >70 year and the administration of additional opioids by other routes were risk factors for the development of respiratory depression [212]. However, the reported incidence of respiratory depression with fentanyl local anaesthetic epidurals of 0.3% [213] is no higher than the incidence of respiratory depression when opioids are administered by other routes. Drug errors whereby the wrong drug is administered epidurally have been reported [214] but fortunately are rare and should be reduced further by using dedicated epidural delivery systems. The reported incidence of serious complications has varied although an estimate of 0.0007% is often quoted. The Third National Audit Project, the largest prospective study of complications after central neuraxial blocks, has helped clarify the incidence of serious complications associated with epidurals [4, 5]. This confirmed that overall (peri-operative, obstetric, paediatric and chronic pain) central nerve blocks were associated with a very low (0.007%) incidence of major complications. The incidence of major complication after epidurals inserted peri-operatively was, however, much higher at 0.02%. The most frequent complications were epidural haematomas [5]. This incidence of major complications after peri-operative epidurals is almost the same as that incidence reported in an earlier Swedish study [215].

Neuroaxial Block and Coagulation

Due to the rarity of spinal epidural hematoma case reports, expert opinion, not scientific evidence from controlled trials, provides the mainstay of recommendations for epidural analgesia in patients receiving antithrombotic medications. This is particularly true for thromboprophylaxis [216]. The risk of an epidural inserted for post-thoracotomy analgesia resulting in a permanent injury or death is approximately 0.02%. Epidural haematomas account for most of this morbidity [4, 5]. Anticoagulants and antiplatelet agents can further increase the risk of vertebral canal haematoma [217, 218] and may increase the risk of epidural abscesses by causing small haematomas that become secondarily infected. All patients receiving thoracic epidural analgesia and patients who have undergone unsuccessful attempts at epidural catheter placement should be monitored regularly for symptoms and signs of vertebral canal haematoma, specifically back pain, motor or sensory changes and urinary retention (if not catheterised). Of these, motor block is the most reliable sign and most sensitive prognostic indicator [219]. Vertebral canal haematoma occurring in the peri-operative period have a poor outcome.

Oral Anticoagulants (Warfarin)

When thoracic epidural analgesia is planned warfarin should be discontinued at least 4–5 days pre-operatively. The INR should be within normal limits prior to placing the epidural catheter to ensure adequate levels of active vitamin K-dependent clotting factors. Haemostasis may not be adequate even with an INR of 1.3 [6]. Warfarin therapy should not be reinstated until after removal of the epidural catheter and the INR should be <1.5 prior to catheter removal.

Antiplatelet Medications

There is considerable variability in patient responses to antiplatelet agents. The increased risk in individual patients may therefore be difficult to quantify, although female sex, advanced age and a history of easily bruising can signify an increased risk. The role of near-patient testing of platelet function prior to neuraxial block needs to be established.

NSAIDs (Including Aspirin)

NSAIDs appear not to increase the risk of vertebral canal haematoma in patients undergoing neuroaxial blockade [6, 220, 221]. Concurrent administration of other haemostasis altering medications does, however, appear to increase the risk of bleeding [6], especially in the case of aspirin. This includes heparin for post-operative thromboprophylaxis [216, 218]. Thus, if feasible, aspirin should be discontinued 5–7 days prior to surgery if central neuraxial blockade and heparin-based DVT prophylaxis is planned.

Thienopyridine Derivatives

These include clopidogrel and ticlopidine. They are potent antiplatelet agents causing irreversible inhibition of ADP-induced platelet aggregation and platelet–fibrinogen binding inhibition. Clopidogrel should be discontinued at least 7 days and ticlopidine at least 10–14 days prior to neuraxial blockade [6].

Herbal (Alternative) Medication [6, 216]

Up to 50% of surgical patients may be taking herbal medications pre-operatively although many do not volunteer this information. Although herbal drugs by themselves probably pose no significant added risk, Garlic, Ginseng and Gingko have raised concern because they are associated with thrombocytopenia, inhibition of platelet aggregation and interaction with vitamin K antagonists. There may be a small increased risk of an epidural haematoma if patients receive heparin for thromboembolism prophylaxis. It is probably wise to actively seek a history of such herbal therapy usage and discontinue it 7 days pre-operatively.

Coronary Stents

An increasing number of patients with coronary artery stents in situ and receiving antiplatelet drugs are presenting for thoracic surgery. After insertion patients receiving bare metal stents require aspirin and clopidogrel for at least 4 weeks. Patients receiving drug eluting stents require aspirin and clopidogrel for at least 12 months. All patients with stents in situ require aspirin for life [7, 9, 222]. Dual-antiplatelet therapy is a contraindication to epidural analgesia [6]. Although discontinuing clopidogrel ≥ 7 days pre-operatively while continuing aspirin may make thoracic epidural feasible, the premature discontinuation of one antiplatelet agent markedly increases the risk of acute peri-operative stent thrombosis with significant cardiac morbidity and mortality [7–9]. Aspirin therapy should rarely be interrupted [9]. The planned duration of post-operative epidural analgesia is also relevant as antiplatelet therapy should be recommended as soon as possible post-procedure as delays may expose the patient to an unacceptable risk of stent thrombosis [7].

Thromboprophylaxis

Subcutaneous unfractionated heparin is effective in reducing the incidence of thromboembolic complications [6, 223]. As there have been only five case reports of vertebral canal haematomata associated with neuraxial blockade in patients receiving subcutaneous unfractionated heparin published in the literature [224–226] subcutaneous heparin in patients with thoracic epidurals in situ appears safe [227]. If subcutaneous heparin is continued for greater than 4–5 days a platelet count is recommended prior to removal of the epidural catheter as heparin-induced thrombocytopenia may occur. Low molecular weight heparins have different biochemical and pharmacological properties to unfractionated heparin including anti-Xa activity [6]. The half life of anticoagulant activity following the administration of a dose of subcutaneous low molecular weight heparin is considerably longer than that following a subcutaneous dose of unfractionated heparin, allowing once daily dosage. In the late 1990s, there were reports of more than 40 cases of vertebral canal hematomata in patients following neuraxial blockade in the United States. This may have been the result of the North American guidelines recommending twice daily dosage, meaning there was effectively no “safe” time in which to perform a block or remove an epidural catheter. Similar clusters of cases of hematomata were not reported in Europe despite extensive experience of regional blockade

concurrent with low molecular weight heparin thromboprophylaxis [228, 229]. This is thought to represent the once daily dosage employed in Europe. However, despite this neuraxial blockade in the presence of low molecular weight heparin thromboprophylaxis is more risky than with unfractionated heparin, especially for epidural catheter techniques [6].

Urinary Retention

Urinary retention is a well-known complication of epidural opioids use [230]. The mechanisms for this include inhibition of the sacral parasympathetic outflow and inhibition of the pontine micturition centre [231]. Epidural morphine-mediated reduction in detrusor muscle function is antagonised by naloxone [232] and in post-hysterectomy patients naloxone can reverse bladder dysfunction without reversing epidural morphine analgesia [233]. However, when given to post-thoracotomy patients receiving thoracic fentanyl bupivacaine epidural analgesia, naloxone reversed the analgesic effects of the epidural without reducing the need for urinary catheterisation [234] and is not recommended for this purpose.

Gastric Emptying

The excellent early analgesia provided by thoracic epidural analgesia enables most patients to resume their normal diet and oral medications a few hours post-thoracotomy. The rate-limiting step for the absorption of most orally administered drugs is gastric emptying. Gastric emptying is variably affected by anaesthesia and surgery [235–237]. Epidural opioids can result in gastric hypomobility. Branches of the T6–T10 sympathetic nerves innervate the stomach [238] and sympathetic blockade of these nerves could hasten gastric emptying. Gastric emptying has been shown to be normal in patients receiving bupivacaine epidural analgesia post-cholecystectomy [237]. For post-thoracotomy patients receiving a fentanyl bupivacaine, thoracic epidural gastric emptying is delayed for >48 h [239]. This delayed gastric emptying may lead to reflux or regurgitation and altered effects of orally administered drugs.

Hypotension

Hypotension is a common clinical occurrence during thoracic epidural analgesia. It is important to appreciate the differences between hypotension due to a lumbar vs. mid-thoracic epidural sympathetic blockade. With lumbar neuraxial blockade, hypotension is primarily due to systemic vasodilation, decreasing cardiac preload and afterload. The hypotension due to thoracic epidural blockade occurs for these two previous reasons and also due to blockade of the cardiac sympathetic supply, T2–T4, which interferes with the heart's ability to increase contractility. Unlike treatment of hypotension during lumbar blockade, hypotension during thoracic epidural blockade will have a limited response to increases of preload and afterload and therefore requires treatment with a β -adrenergic or mixed agonist (e.g. ephedrine, dopamine, etc.) to increase cardiac contractility and restore cardiac output [240].

Shoulder Pain

Ipsilateral shoulder pain is common in patients receiving effective thoracic epidural analgesia and occurs occasionally in patients receiving paravertebral blocks, but is rare in patients not receiving nerve blocks for post-thoracotomy analgesia. The reported incidence of ipsilateral shoulder pain in patients receiving thoracic epidural analgesia varies from 42 to 86% [18, 19, 109, 142, 241]. This shoulder pain is often described by patients as an ache, usually of moderate to severe intensity, and lasts for a few days. Early explanations of this shoulder pain were that it was related to the transection of a major bronchus although no mechanism was suggested [18]. Other early explanations included stretching of the brachial plexus or the shoulder joint as a result of the intra-operative positioning and distraction of the posterior thoracic ligaments by surgical retractors [17]. Recent studies have helped explain the pathogenesis of this pain. A double-blind study of patients who had developed ipsilateral post-thoracotomy shoulder pain in which patients were given either bupivacaine or saline to block the suprascapular nerve found that blocking the suprascapular nerve did not affect the incidence of pain [241]. This makes intra-operative shoulder distraction an unlikely cause of ipsilateral post-thoracotomy shoulder pain. A placebo-controlled study of the administration of bupivacaine through the basal drain found that bupivacaine was not effective in reducing ipsilateral post-thoracotomy shoulder pain [142]. Irritation of the diaphragmatic pleura by a basal chest drain is therefore unlikely to be a significant cause of ipsilateral post-thoracotomy shoulder pain. A placebo-controlled study in which the periphenic fat pad, at the level of the diaphragm, was infiltrated with either lidocaine or saline intraoperatively reduced the early incidence of ipsilateral post-thoracotomy shoulder pain from 85 to 33% [19] (see Fig. 46.14).

This marked reduction in the incidence of ipsilateral post-thoracotomy shoulder pain with phrenic nerve infiltration was confirmed in a later study [242]. The phrenic nerve must therefore be importantly involved in the pathogenesis of ipsilateral

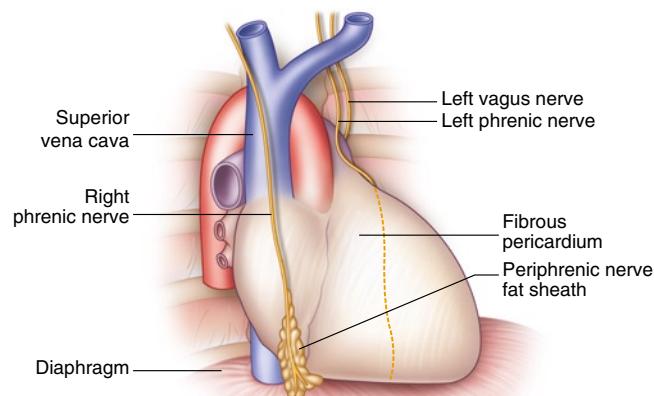


FIG. 46.14. Diagram to illustrate the site of the periphenic nerve fat sheath for phrenic nerve blocks (modified with permission from Gosling et al. [278] and Scawn et al. [19]).

post-thoracotomy shoulder pain. The phrenic nerve supplies sensory branches to the mediastinal pleura, the fibrous pericardium, the parietal layer of the serous pericardium and the pleura related to the central part of the diaphragm. In most patients, the likely explanation of ipsilateral post-thoracotomy shoulder pain is irritation of the pericardium, mediastinal and diaphragmatic pleural surfaces resulting in pain referred to the shoulder via the phrenic nerve. In a few patients with ipsilateral post-thoracotomy shoulder pain and an apical chest drain extending to the apex of the chest cavity, withdrawal of the chest drain by a few centimetres relieves the pain. This implies that irritation of the apical pleura by the chest drain is another cause of ipsilateral post-thoracotomy shoulder pain.

Recent studies have helped guide the treatment of ipsilateral post-thoracotomy shoulder pain. The pain is resistant to epidural boluses [76] and intravenous opioids [19]. Pre-operative gabapentin [109] is similarly ineffective. Effective treatment options for ipsilateral post-thoracotomy shoulder pain include acetaminophen [93], non-steroidal anti-inflammatory agents [18, 76], direct intra-operative phrenic nerve blocks [19, 242] and indirect post-operative phrenic nerve blocks [243, 244]. Rectal acetaminophen is safe and moderately effective [93] although personal experience suggests intravenous acetaminophen to be more effective. The use of acetaminophen orally, rectally or intravenously to treat ipsilateral post-thoracotomy shoulder pain is recommended. Non-steroidal anti-inflammatory agents are effective in controlling ipsilateral post-thoracotomy shoulder pain [18, 76] and personal experience suggests that they are more effective than acetaminophen. The well-known side effects of NSAIDs are, however, a particular concern in the often old and debilitated patients who have undergone thoracic surgery and the risks should be assessed before their use. Intra-operative phrenic nerve blocks are effective. The short duration of effect with lidocaine [19] can be extended by the use of ropivacaine [242] but patient selection is important as the resultant unilateral diaphragmatic paresis can further impair ventilation. Phrenic nerve blocks should be considered for patients in whom post-operative pulmonary function is not a concern and for patients undergoing a pneumonectomy. In post-pneumonectomy patients, the unilateral loss of diaphragmatic function has limited effects on ventilation and may have an additional benefit of helping to reduce the pneumonectomy space. Post-operative interscalene brachial plexus blocks have been shown to be effective in treating ipsilateral post-thoracotomy shoulder pain in case reports [243] and in a prospective study [244]. The phrenic nerve block that is a side effect of interscalene brachial plexus block [245] almost certainly explains the blocks effectiveness. Because of the potential complications associated with this block we recommend that interscalene brachial plexus blocks be considered only in patients with severe ipsilateral post-thoracotomy shoulder pain and adequate pulmonary reserve. Although a stellate ganglion block may be effective in treating ipsilateral post-thoracotomy shoulder pain [246], its use for this purpose is not recommended.

Techniques for Specific Procedures

Sternotomy

A sternotomy can be used to provide access for a range of surgical procedures including the resection of anterior mediastinal tumours. At closure the divided sternum is usually internally fixed with wire. This fixation restricts bone movement and limits pain. Adequate post-sternotomy analgesia can usually be achieved with a morphine IV-PCA system supplemented when appropriate by non-opioid analgesics. Local anaesthetic wound infiltration can reduce opioid consumption [247] and should be considered. Continuous wound infiltration via deep and/or subcutaneous catheters may be more effective but evidence of effectiveness is limited, with some studies showing no benefit [248]. Thoracic epidurals can provide very effective post-sternotomy analgesia. The catheter should be sited at a higher level (T3/T4) than for a thoracotomy (T6/T7) and any paresthesia of the medial surface of the arms detected early, to enable a timely reduction in the epidural infusion rate to limit the risk of bilateral phrenic nerve (C4–C5) blocks. Thoracic epidural analgesia should be considered for patients with poor lung function undergoing bilateral pulmonary procedures via a sternotomy (e.g. volume reduction surgery). A parasternal local anaesthetic block can reduce opioid requirements [249] and should be considered in patients with poor lung function in whom epidural anaesthesia is contraindicated.

Video-Assisted Surgery

The limited incision may limit post-operative pain. The appropriate analgesia depends in part on the nature of the surgery undertaken. Thoracic epidural analgesia is usually provided for patients undergoing VAT lung volume reduction surgery and may be advantageous in patients undergoing minimally invasive oesophagectomies [250]. Paravertebral blocks and/or an IV-PCA system may be appropriate for patients undergoing VAT lung resections. Minimal analgesia may be required after VAT pleural biopsies or sympathectomies.

Open Thoracotomy

A large number of pain management techniques have been described for open thoracotomy patients. These have included the administration of local anaesthetics, opioids and other drugs to provide intercostal nerve blocks [128–130], interpleural blocks [136–139], paravertebral blocks [162, 251, 252], lumbar epidural analgesia [253–255], thoracic epidural analgesia [1, 2, 178, 185, 186], intrathecal analgesia [166–172] and systemic analgesia [10]. In addition, the non-pharmacological techniques of cryoanalgesia [123, 124] and TENS [116–122] have been used. Good post-thoracotomy pain control is difficult to achieve without regional anaesthesia (or multiple nerve blocks) and it is recommended that a regional anaesthetic technique be used alone, or in combination with

systemic analgesics, to provide post-thoracotomy analgesia. As apart from paravertebral blocks all other regional analgesic techniques are inferior to thoracic epidural analgesia [10], the choice of regional anaesthetic technique is usually between thoracic epidural analgesia and a paravertebral block.

Thoracic epidurals usually provide post-thoracotomy analgesia with an epidural mixture of opioids and local anaesthetics; patients usually receive no systemic analgesics apart from perhaps acetaminophen or NSAIDs for shoulder pain. In contrast, paravertebral blocks are usually supplemented with systemic morphine, NSAIDs and other systemic analgesics for at least the early post-operative period. These differences are important in the interpretation of studies that have compared thoracic epidural analgesia and paravertebral blocks. A meta-analysis published in 2006 included 10 trials with 520 enrolled patients [11]. In six of the trials, the epidural group received higher concentrations of epidural local anaesthetics than generally used [14] or recommended. It is well known that the incidence of post-operative hypotension is increased when higher concentrations of epidural local anaesthetics are used. Similarly, in only four of the trials were epidural local anaesthetics supplemented with opioids used as is recommended and usual practice [14]. Notwithstanding these limitations, it was concluded that the two techniques provided comparable analgesia and that pulmonary complications were lower in the paravertebral group [11]. Similarly, a 2008 review of regional techniques for post-thoracotomy analgesia found that a continuous thoracic epidural infusion of local anaesthetics and opioids provided the most consistently effective analgesia [10]. However, when compared to systematic analgesia, thoracic paravertebral blocks, but not thoracic epidural analgesia, reduced the incidence of pulmonary complications [10]. In practice both techniques have advantages in particular patients and the acquisition of expertise in both techniques is recommended. For patients with borderline predicted post-operative lung function, good early analgesia and the ability to co-operate with lung recruitment manoeuvres immediately post-operatively may be critical. Correctly sited thoracic epidurals provide reliable good early analgesia with minimal sedation and their use in this scenario is recommended. A retrospective analysis of one institute's data showed that a pre-operative FEV_1 of less than 60% predicted was an independent risk factor for the development of post-thoracotomy pulmonary complications and mortality. The use of thoracic epidural analgesia was associated with reduced pulmonary complications and a reduced mortality in patients with an $FEV_1 < 60\%$, although no patients were reported to have received a paravertebral block [256] (see Fig. 46.15). A prospective 1-year observational study of pneumonectomies in the United Kingdom found epidural analgesia to be a significant associate of poor outcome [257].

For patients with good pulmonary function undergoing limited lung resection, early analgesia may be less critical and paravertebral analgesia may enable earlier mobilisation and shorten hospital stays. For most patients, the decision is less clear cut and consideration of the relative risks and benefits of

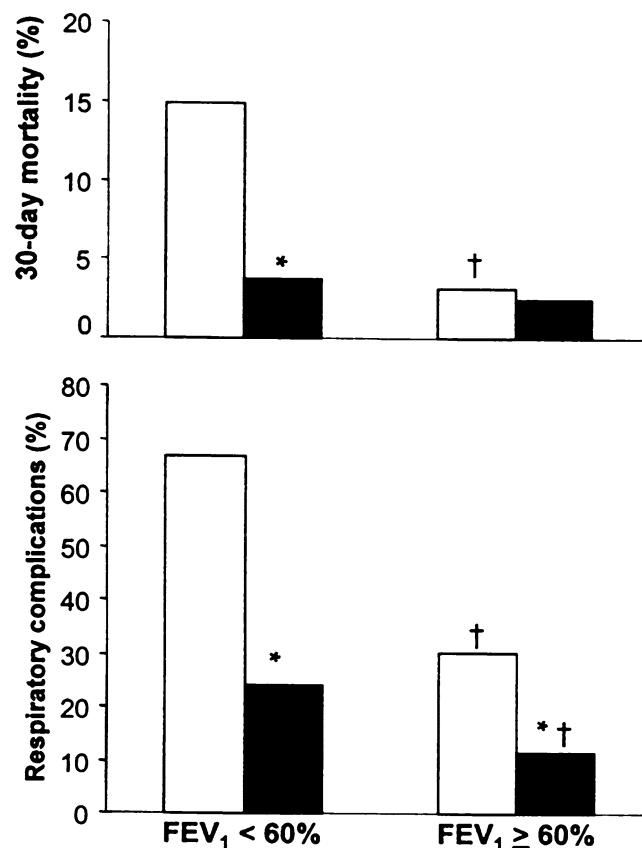


FIG. 46.15. Thirty-day mortality rate (top) and incidence of respiratory complications (bottom) according to pre-operative FEV_1 (<60% or $\geq 60\%$) and type of analgesic regimen: without thoracic epidural analgesia (white bars) or with thoracic epidural analgesia (black bars). * $p < 0.05$, compared with group without thoracic epidural analgesia; † $p < 0.05$, compared with group $FEV_1 \geq 60\%$ (FEV_1 , forced expiratory volume in 1 s) (this figure was published in Licker et al. [256]. © Elsevier [2006]).

TABLE 46.3. Factors influencing choice of paravertebral block or thoracic epidural.

Favours thoracic epidural	Favours paravertebral block
Poor PFTs	Good PFTs
Extensive lung resection	Limited lung resection
Chest wall involvement	Sepsis
Non-steroidal anti-inflammatory drugs (NSAIDs) contraindicated	Impaired coagulation
Patient preference	Patient preference
	Fixed spinal deformity
	Anaesthetised patient

PFTs Pulmonary function tests

the two techniques should be made for the particular patient (see Table 46.3). For patients for whom neither thoracic epidural or paravertebral blocks is appropriate consideration should be given to the use of intercostal nerve blocks or pre-operative intrathecal opioids.

Oesophageal Surgery

Post-operative pain can be very severe after open oesophageal surgery and thoracic epidural analgesia is usually used to provide post-operative analgesia for these patients. For patients undergoing a minimally invasive oesophagectomy, the combination of an IV-PCA system, a paravertebral block and non-opioid analgesics is frequently used. Recent work, however, found an increased mortality in patients undergoing a minimally invasive oesophagectomy without a thoracic epidural [250] and a thoracic epidural should be considered for all patients scheduled to undergo an oesophagectomy. Post-oesophagectomy thoracic epidural analgesia probably has benefits in addition to providing good analgesia. In non-randomised studies comparing systemic opioids with epidural analgesia after open oesophageal surgery, patients receiving epidural analgesia had fewer respiratory complications [258], spent less time in intensive care [258, 259] and had a lower mortality [258, 260, 261]. In 1994, Watson and Allen [261] stated that in their experience “the routine use of thoracic epidural analgesia has been the most significant advance in the management of patients with oesophageal cancer during the past 15 years”. Similarly, Law et al. [262] attributed their low post-oesophagectomy complication rate to thoracic epidural analgesia and said “Perhaps the most important advance in peri-operative care in oesophagectomy in the 1990s was the use of epidural analgesia, which was shown to reduce complications and death rate”. Thoracic epidurals may decrease the incidence of anastomotic leakage post-oesophagectomy [263]. Ischemia at the anastomotic end of the newly formed gastric tube is a major cause of anastomotic leaks post-oesophagectomy [264]. A relationship between low Doppler determined blood flow at the anastomotic site and subsequent anastomotic leakage has been shown [265]. Although intra-operative epidural boluses can cause hypotension and reduced blood flow to the anastomotic end of the gastric tube [266], a study using continuous post-operative thoracic epidurals found epidurals to be associated with minimal hypotension and an increased distal conduit blood flow [267]. We recommend that “anesthesiologists should be cautious in accepting intra-operative hypotension secondary to epidural administration in patients undergoing esophagectomy” [266]. For patients undergoing open oesophageal surgery in whom epidural analgesia is inappropriate or contraindicated consideration should be given to the use of a continuous paravertebral block as they have been reported to provide reasonable analgesia when supplemented by systemic analgesics [268].

Opioid Tolerant Patients

Opioid tolerant patients presenting for thoracic surgery include patients with malignant diseases receiving opioids for pain, a rapidly increasing group of patients with non-malignant

disease receiving opioids chronically for pain management, opioid-dependent substance abusers and former addicts on long-term maintenance programmes. The principles of treatment are similar for all groups but opioid substance abusers may present additional challenges due to their psychological problems, dependency on other substances (e.g. alcohol) and concomitant infectious diseases (e.g. tuberculosis, human immunodeficiency virus) which may affect the delivery of anaesthesia.

Achieving good post-operative analgesia in patients who are chronically receiving opioids is frequently difficult and these patients may experience more post-operative pain. Patients should when practical be involved in the plans for their post-operative pain management. Abrupt cessation of opioids can result in an acute opioid withdrawal syndrome and should be avoided. Naltrexone, a long acting opioid antagonist used to help prevent relapse in detoxified former opioid dependent patients, should be discontinued a few days before surgery. The route and usual daily dose of opioids should be established, and for patients scheduled for major surgery and an equivalent intravenous dose of morphine estimated. Unfortunately, variability in the pharmacokinetics, pharmacodynamics, route of administration and daily opioid consumption make estimating a morphine equivalent dose difficult. For opioid naïve patients, receiving an IV-PCA for post-thoracotomy analgesia, a background opioid infusion is usually not appropriate. Opioid-dependent patients however should, in addition to any demand opioids, receive at least 50% of their usual dose of opioid orally, or if this is not appropriate, as a background infusion throughout the peri-operative period. Most patients undergoing open thoracic surgery benefit from the addition of a regional anaesthetic technique and/or the addition of adjunctive pharmacologic agents to their opioids. Thoracic epidurals can provide excellent post-thoracotomy analgesia in opioid tolerant patients and their use is recommended. The use of a lipophilic opioid local anaesthetic mixture is recommended. Lipophilic opioids local anaesthetic mixtures have been shown to provide pain control that is superior to morphine local anaesthetic mixtures in opioids tolerant patients perhaps because analgesic effects are exerted at lower receptor occupancy [269, 270]. An alternative for patients scheduled to receive significant amounts of opioids by other routes is the use of a plain local anaesthetic epidural solution. Where thoracic epidural use is inappropriate a surgically placed catheter and paravertebral infusion is recommended. Non-opioid adjuvant analgesic agents should also be considered. The use of NSAIDs or COX-2 inhibitors is particularly appropriate for opioid tolerant patients and their use is recommended although there are few studies evaluating their use in opioid-dependent patients.

For a few patients, parenteral opioids may be the most appropriate means of providing post-operative analgesia. Despite earlier concerns of increasing addiction and manipulative behaviour, the use of intravenous IV-PCA systems to

control pain in substance abusers is now generally considered acceptable, if this system is used appropriately. Predicting the postoperative opioid requirement for opioid-dependent patients is difficult. Opioid tolerant patients are more likely to become sedated than opioid naïve patients despite having higher pain scores [271]. Swenson et al noted that during drug administration there is initially a disparity between the plasma concentration and the concentration of the drug at its site of action (effect site concentration). They describe a method of determining the effect site concentration of fentanyl at the threshold of respiratory depression in individual patients using simulation software and a fentanyl infusion. After determining the effect site concentration of fentanyl at the threshold for respiratory depression an hourly fentanyl administration rate that will result in 30% of this effect site concentration is calculated. Utilising an intravenous PCA system half of this calculated fentanyl dose can be administered as a background infusion while the remaining 50% is programmed for demand administration as boluses with a 15-min lockout period. They recommend that the regimen be reviewed at 4 hourly intervals and adjustments made based on the number of demand boluses administered, the level of consciousness and the respiratory rate [272]. Methadone, a NMDA receptor antagonist which can activate α adrenergic receptors and a different range of μ receptors subtypes to morphine, is regarded as the intravenous PCA opioid of choice for opioid-dependent patients by some authors [273]. Consideration should be given to using a methadone IV-PCA system in opioid-dependent patients whose post-operative pain is refractory to large doses of systemic morphine. The administration of a low dose ketamine infusion should be considered particularly in patients for whom regional anaesthetic techniques are not planned. The literature suggests that for opioids tolerant patients an intra-operative bolus of ketamine ($\sim 0.25 \text{ mg kg}^{-1}$) should be followed by an intravenous infusion ($\sim 2 \text{ } \mu\text{g kg}^{-1} \text{ min}^{-1}$) continued for a few days [274]. Although adding ketamine to morphine delivered via an IV-PCA has been described [101] this is not recommended in opioids tolerant patients because the large and unpredictable opioids requirements may result in the administration of excessive doses of ketamine with the associated psychotropic side effects [274].

Conclusion

Pain control after surgery is central to the anaesthetic management of patients undergoing thoracic surgery. The provision of good post-operative analgesia is of itself important and is regarded by some as the core business of anaesthesia and a fundamental human right [275]. Effective analgesia can reduce pulmonary complications and mortality [256]. It is unlikely that a single technique will optimally fulfil these objectives for all patients. Analgesia should be tailored to the

specific patient undergoing a specific procedure and aim to minimise mortality, patient suffering, pulmonary complications and other morbidity. Experience with a wide range of analgesic techniques is helpful as it enables the implementation of an appropriate technique. For open thoracotomies most patients are best managed by a combination of regional analgesia and opioids, sometimes supplemented with non-opioid analgesics. There is no role for interpleural blocks or cryoanalgesia in adults. Lumbar epidural analgesia, intrathecal opioids or intercostal nerve blocks should usually be considered only if neither thoracic epidural analgesia or paravertebral blocks are possible. At present the dilemma for thoracic anaesthetists and their patients scheduled to undergo a thoracotomy is the choice between thoracic epidural analgesia and paravertebral block. It has been well established that thoracic epidurals produce excellent post-thoracotomy analgesia. There is also evidence that thoracic epidural analgesia reduces post-thoracotomy pulmonary complication [256] although these advantages have not been shown in recent analyses particularly when thoracic epidurals are compared with paravertebrals [10, 11]. Thoracic epidurals are associated with a risk of permanent injury and this risk is orders of magnitude greater than the risks associated with lumbar epidural administered in parturients [5]. The most frequent disabling complications are epidural haematomas [5]. An increasing number of patients presenting for thoracic surgery are receiving drugs that affect coagulation, not all of which are prescribed. Current anticoagulant and antiplatelet medication increases the risk of epidural by an unquantified amount. Impaired coagulation is less of a contraindication to thoracic paravertebrals, particularly when they are inserted under direct vision. Serious complications are rare with paravertebrals. Recent meta-analysis and systemic analysis have suggested that paravertebrals are more effective at reducing pulmonary complications than thoracic epidurals [10, 11]. However, only a limited number of patients have been enrolled in studies comparing paravertebrals with thoracic epidural analgesia and many received suboptimal epidural solutions. It is anticipated that in the future additional data on the relative benefits of opioid/local anaesthetic thoracic epidural vs. paravertebral with systemic opioids will aid the difficult decision on epidural insertion for high risk patients who are also at increased risk of epidural related complications. In the future, the development of clinically useable ultra-long acting local anaesthetics might enable significant further advances to be made in the provision of post-thoracotomy analgesia.

Addendum

Editors note: For the reader's further information, Figs. 46.16, and 46.17 are protocols for Patient Controlled Epidural Analgesia after thoracic or upper abdominal surgery from the Toronto General Hospital.

FIG. 46.16. (a, b) Standard anaesthesiologist order sheets for thoracic epidural analgesia infusions with patient-controlled boluses p.r.n., following thoracic or upper abdominal surgery (images courtesy of the Toronto General Hospital).

a

While on PCEA device, the patient is to receive **No** further supplemental Opioids **or** other CNS depressants unless approved by the Anaesthesia/Acute Pain Service.

Only the patient should press the PCEA delivery pendant unless otherwise directed by the APS. (Check appropriate box(es) and complete orders as required)

1. MONITORING:
Patient Monitoring as per PCEA Flowsheet Form No. 2444

2. MEDICATIONS: Common PCEA Orders

Single dose opioid injection:
 Epidural Spinal/Intrathecal
 Operating Room Dose: Drug _____ mg Time _____ hrs

T 4 – 6 Level: Bupivacaine 0.1% and Hydromorphone 0.015 mg/mL in 250 mL normal Saline; Epidural Rate 4 mL/h; Bolus dose 2 mL; Lockout period 20 min; 4 h limit 40 mL

T 7-11 Level: Bupivacaine 0.1% and Hydromorphone 0.015 mg/mL in 250 mL normal Saline; Epidural Rate 5 mL/h; Bolus dose 3 mL; Lockout period 20 min; 4 h limit 50 mL

T 12 – L4 Level: Bupivacaine 0.1% and Hydromorphone 0.015 mg/mL in 250 mL normal Saline; Epidural Rate 8 mL/h; Bolus dose 3 mL; Lockout period 20 min; 4 h limit 60 mL

T 4 – 6 Level: Ropivacaine 0.2% in 200 mL Normal Saline; Epidural Rate 4 mL/h; Bolus dose 2 mL; Lockout period 20 min; 4 h limit 40 mL

T 7-11 Level: Ropivacaine 0.2% in 200 mL Normal Saline; Epidural Rate 5 mL/h; Bolus dose 3 mL; Lockout period 20 min; 4 h limit 50 mL

T 12 – L4 Level: Ropivacaine 0.2% in 200 mL Normal Saline; Epidural Rate 8 mL/h; Bolus dose 3 mL; Lockout period 20 min; 4 h limit 60 mL

Associated Medications

Dimenhydrinate (Gravol®) 25-50 mg IV-int / IM q 3 h PRN for nausea
 Granisetron (Kytril®) 1 mg IV-int q 24 h x 2 doses PRN for nausea
 Diphenhydramine (Benadryl®) 25-50 mg IV-int q 3 h PRN for pruritis

b

(Check appropriate box(es) and complete orders as required)

Other Epidural Solutions:

Bupivacaine 0.1% and Hydromorphone 0.015 mg in 250 mL normal Saline; Epidural Rate _____ mL/h; Bolus dose _____ mL; Lockout period _____ min; 4 h limit _____ mL

Bupivacaine 0.1% and Fentanyl 4 mcg/mL in 250 mL normal Saline; Epidural Rate _____ mL/h; Bolus dose _____ mL; Lockout period _____ min; 4 h limit _____ mL

Ropivacaine 0.2% in 200 mL Normal Saline; Epidural Rate _____ mL/h; Bolus dose _____ mL; Lockout period 20 min; 4 h limit _____ mL

NSAID

Ketorolac 15 mg IV q 8 h x 6 doses
 Ketorolac 15 mg IV q 6 h x 8 doses
 Celecoxib 200 mg PO tablet bid x 10 doses

Acetaminophen

D/C all other Acetaminophen orders.
 Max daily doses of acetaminophen from all sources = 4 g (i.e., 12 x 325 mg, 8 x 500 mg, 6x650 mg)

Acetaminophen 1000 mg PO tablet q 6 h x 8 doses
 Acetaminophen 1000 mg PO tablet q 6 h X 20 doses then q 6 h PRN
 Acetaminophen Suppository 1300 mg PR q 8 h X 6 doses
 Acetaminophen 650 mg PO tablet q 6 h X 8 doses
 Acetaminophen 650 mg PO tablet q 6 h X 20 doses then q 6 h PRN
 Acetaminophen 960 mg elixir via feeding tube q 6 h X 8 doses

(For TGH Only) When Epidural Removed by Anesthesia (APS), start oral analgesics as below:

(Percocet®) Oxycodone 5 mg w/ Acetaminophen 325 mg 1 – 2 tabs PO q 3 H PRN (max 12 tablets/24 h)
 (Oxy IR®) Oxycodone Immediate Release 5 – 10 mg PO tablet q 2 h PRN
 (Statex®) Morphine Immediate release 10 mg PO tablet q 3 h PRN
 (Statex®) Morphine Immediate release 10-20 mg PO tablet / feeding tube solution q 3 h PRN
 Hydromorphone elixir 2-4 mg PO tablet / feeding tube solution q 3 h PRN
 Acetaminophen 640 mg elixir via feeding tube q 4 h PRN

When Patient tolerating fluids well, start following Bowel Medication:

Docusate Sodium (Colace®) 100 mg PO/elixir via feeding tube BID
 Senokot® 2 tabs (8.6 mg Senna/tablet) PO q 12 h

Anesthesia (APS) will remove epidural Catheter. Maintain IV access for 12 hours after epidural catheter removal

MONITORING:

- i) a) Two RN's will check and verify the initial epidural settings and document on Epidural Analgesia Flowsheet.
b) RN's will check and verify the epidural settings every shift and document on Epidural Analgesia Flowsheet.
- ii) **Single Dose Opioid Injection**
Respiratory rate and sedation scale q 1 h for 24 hours.
- iii) **Epidural Combined Local Anesthetic and Opioid Infusion**
 - a) **Activity:** Check postural blood pressure, pulse and sensory/motor block before getting up.
 - b) Respiratory rate and sedation scale q 2 h for 24 hours, then q 4 h if infusion rate is not increased.
If epidural rate increased respiratory and sedation scale q 2 h x 24 hours.
 - c) **Vital Signs:** a) 5 min after loading dose of local and/or narcotic then q 30 min x 2, then q 4 h. b) q 4 h during continuous infusion.
 - d) Sensory/motor block level q 4 h while epidural in situ.
 - e) Once Epidural catheter removed by APS monitor motor function in lower limbs and presence/absence of back pain near epidural insertion site q 4 h for 24 hours while patient in hospital: **Notify APS/Anesthesia immediately of any motor deficits or back pain**
- iv) **CALL THE ACUTE PAIN SERVICE FOR:**
 - a) Inadequate pain control
 - b) Blood Pressure Systolic less than 90 mm Hg
 - c) Pulse less than 50 beats per minute.
 - d) Sedation score of 3 (somnolent, difficult to arouse).
 - e) Respiratory Rate less than 10.
 - f) Increased sensory or motor block, with local anesthetic.
 - g) Epidural catheter problems.

- Only the patient should press the PCEA delivery pendant unless otherwise directed by the APS
- Maintain IV access for 12 hrs after epidural catheter removed.

PAIN SCORE Q4H	SEDATION SCALE (q2h x 24 hours then q4h)	SENSORY LEVEL (q4h x 24 hrs then q8h) Refer to Sensory Dermatomes on reverse	MOTOR STRENGTH IMPAIRMENT SCALE (q4h while epidural insitu then q4h x 24h after epidural removed)	PRURITUS/NAUSEA/VOMITING
0 no pain	10 worst pain possible	0 = Alert 1 = Mild (occ. drowsy, easy to arouse) 2 = Moderate, (freq. drowsy, easy to arouse) 3 = Severe, (somnolent, difficult to arouse) S = Normal sleep (ease to arouse)	0 = No sensory deficit	0 = None 1 = Mild, no rx needed 2 = Moderate, rx effective 3 = Treatment not effective
RESPIRATORY RATE (q2h x 24 hrs then q4h x 24 hourS)				URINARY RETENTION F = Foley O = No retention, voiding well *(red) = See Clinical Notes for in and out cath

FIG. 46.17. Nursing protocol for monitoring patients with thoracic epidural infusions in the intensive care unit or on the post-operative surgical ward (image courtesy of the Toronto General Hospital).

Clinical Case Discussion

Case

A 39-year-old man is scheduled for bronchoscopy and right lower lobectomy. He presented to his family doctor 4 months earlier with hemoptysis, diagnosis was delayed because of his frequent non-attendance. A CT-guided fine needle biopsy established the diagnosis as non-small cell carcinoma. He remains a heavy smoker of both marijuana and tobacco and has a 12-year history of heroin addiction. He is presently maintained on oral methadone but admits to occasional intravenous heroin use. Past medical history includes an exploratory right thoracotomy for a knife wound to the chest 5 years ago but no significant illnesses. He is very concerned about post-thoracotomy pain, stating that he suffered greatly after his previous thoracotomy. Clinical examination reveals a thin clubbed man who is very anxious. Pulmonary function tests show a FEV₁ of 65% predicted and a DLCO of 68% predicted. A full blood count, renal function and clotting screen are normal.

Questions

- What additional information might be useful in planning his anaesthetic?
 - Current dose of methadone (substantiated by primary care physician or rehabilitation unit).
 - Ability to tolerate NSAIDs.
 - Intravenous drug use associated infectious diseases status (HIV, Hep C and Hep B).

- How will his long-term opioid intake affect his postoperative analgesia?
 - Tolerance to opioid analgesics impacts on the ability to treat acute pain adequately and he may experience more post-operative pain.
 - Need for maintenance dose of opioids, either orally or by infusion to avoid acute withdrawal.
- What are the post-operative analgesic options?
 - Establish the appropriate route and equivalent dose of the opioid to be administered peri-operatively. Ensure patient receives at least 50% of the equivalent dose to avoid acute withdrawal symptoms. Use a multimodal approach with a regional technique combined with regular acetaminophen and NSAIDs.
 - Choice of regional technique includes thoracic epidural or paravertebral and would be influenced by factors as given in Table 46.3 but a thoracic epidural with a lipophilic opioid offers the best analgesic option.
 - Consideration of gabapentin pre-operative as a single oral dose.
 - If a regional technique is not possible, a ketamine bolus in theatre followed by a ketamine infusion supplemented to an opioid IV-PCA system.

References

1. Griffith DPG, Diamond AW, Cameron JD. Postoperative epidural analgesia following thoracic surgery: a feasibility study. Br J Anaesth. 1975;47:48-55.

2. Shuman RL, Peters RM. Epidural anesthesia following thoracotomy in patients with chronic obstructive airway disease. *J Thorac Cardiovasc Surg*. 1976;71:82–8.
3. Cook TM, Riley RH. Analgesia following thoracotomy: a survey of Australian practice. *Anaesth Intensive Care*. 1997;25:520–4.
4. Cook TM, Counsell D, Wildsmith JA; Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth*. 2009;102:179–90.
5. Counsell D. Complications after perioperative central neuraxial blocks. In: The Third National Audit Project (NAP3), editor. Major complications of central neuraxial block in the United Kingdom. London: The Royal College of Anaesthetists; 2009. p. 101–11.
6. Horlocker TT, Wedel DJ, Benzon H, et al. Regional anesthesia in the anticoagulated patient: defining the risks (The Second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). *Reg Anesth Pain Med*. 2003;28:172–97.
7. Howard-Alpe GM, de Bono J, Hudsmith L, et al. Coronary artery stents and non-cardiac surgery. *Br J Anaesth*. 2007;98:560–74.
8. Chassot PG, Delabys A, Spahn DR. Perioperative antiplatelet therapy: the case for continuing therapy in patients at risk of myocardial infarction. *Br J Anaesth*. 2007;99:316–28.
9. Newsome LT, Weller RS, Gerancher JC, et al. Coronary artery stents: II. Perioperative considerations and management. *Anesth Analg*. 2008;107:570–90.
10. Joshi GP, Bonnet F, Shah R, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. *Anesth Analg*. 2008;107:1026–40.
11. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy – a systematic review and meta-analysis of randomized trials. *Br J Anaesth*. 2006;96:418–26.
12. Eghert LD, Battit GE, Welch CE, Bartlett MK. Reduction of postoperative pain by encouragement and instruction of patients. *N Engl J Med*. 1964;270:825–7.
13. Anonymous. The report of the Public Inquiry into children's heart surgery at the Bristol Royal Infirmary 1984–1995: learning from Bristol. London: TSO; 2001.
14. Pennefather SH, Gilby S, Danecki A, Russell GN. The changing practice of thoracic epidural analgesia in the United Kingdom: 1997–2004. *Anaesthesia*. 2006;61:363–9.
15. Loan WB, Morrison JD. The incidence and severity of postoperative pain. *Br J Anaesth*. 1967;39:695–8.
16. Macintosh RR, Mushin WW. Anaesthetics research in wartime. *Medical Times*. 1945;253–5.
17. Mark JBD, Brodsky JB. Ipsilateral shoulder pain following thoracic operations. *Anesthesiology*. 1993;79:192.
18. Burgess FW, Anderson DM, Colonna D, Sborov MJ, Cavanaugh DG. Ipsilateral shoulder pain following thoracic surgery. *Anesthesiology*. 1993;78:365–8.
19. Scawn ND, Pennefather SH, Soorae A, Wang JY, Russell GN. Ipsilateral shoulder pain after thoracotomy with epidural analgesia: the influence of phrenic nerve infiltration with lidocaine. *Anesth Analg*. 2001;93:260–4.
20. Kirchner A, Birklein F, Stefan H, Handwerker HO. Left vagus nerve stimulation suppresses experimentally induced pain. *Neurology*. 2000;55:1167–71.
21. Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology*. 2004;101:212–7.
22. Bohn LM, Gainetdinov RR, Lin FT, Lefkowitz RJ, Caron MG. Mu-opioid receptor desensitization by beta-arrestin-2 determines morphine tolerance but not dependence. *Nature*. 2000;408:720–3. *vm* 1997;278:58–63.
23. Nestler EJ, Aghajanian GK. Molecular and cellular basis of addiction. *Science*. 1997;278:58–63.
24. Nestler EJ. Molecular basis of long-term plasticity underlying addiction. *Nat Rev Neurosci*. 2001;2:119–28.
25. Mayer DJ, Mao J, Holt J, Price DD. Cellular mechanisms of neuropathic pain, morphine tolerance, and their interactions. *Proc Natl Acad Sci USA*. 1999;96:7731–6.
26. Compton P, Charuvastra VC, Kintaudi K, Ling W. Pain responses in methadone-maintained opioid abusers. *J Pain Symptom Manage*. 2000;20:237–45.
27. Laulin JP, Célèrier E, Larcher A, Le Moal M, Simonnet G. Opiate tolerance to daily heroin administration: an apparent phenomenon associated with enhanced pain sensitivity. *Neuroscience*. 1999;89:631–6.
28. Crile GW. The kinetic theory of shock and its prevention through anoci-association (shockless operation). *Lancet*. 1913;185:7–13.
29. Woolf CJ. Evidence for a central component of post-injury pain hypersensitivity. *Nature*. 1983;306:686–8.
30. Kissin I. Preemptive analgesia. *Anesthesiology*. 2000;93:1138–43.
31. Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. *Anesthesiology*. 2002;96:725–41.
32. Bong CL, Samuel M, Ng JM, Ip-Yam C. Effects of preemptive epidural analgesia on post-thoracotomy pain. *J Cardiothorac Vasc Anesth*. 2005;19:786–93.
33. Hurley RW, Adams MC. Sex, gender, and pain: an overview of a complex field. *Anesth Analg*. 2008;107:309–17.
34. Riley III JL, Robinson ME, Wise EA, Myers CD, Fillingim RB. Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain*. 1998;74:181–7.
35. Pickering G, Jourdan D, Eschalier A, Dubray C. Impact of age, gender and cognitive functioning on pain perception. *Gerontology*. 2002;48:112–8.
36. Gijsbers K, Nicholson F. Experimental pain thresholds influenced by sex of experimenter. *Percept Mot Skills*. 2005;101: 803–7.
37. Sullivan MJ, Rodgers WM, Kirsch I. Catastrophizing, depression and expectancies for pain and emotional distress. *Pain*. 2001;91:147–54.
38. Keefe FJ, Lefebvre JC, Egert JR, Affleck G, Sullivan MJ, Caldwell DS. The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. *Pain*. 2000;87:325–34.
39. Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology*. 2009;111:657–77.
40. Bellville JW, Forrest Jr WH, Miller E, Brown Jr BW. Influence of age on pain relief from analgesics. A study of postoperative patients. *JAMA*. 1971;217:1835–41.
41. Yokoyama M, Hanazaki M, Fujii H, et al. Correlation between the distribution of contrast medium and the extent of blockade during epidural anesthesia. *Anesthesiology*. 2004;100:1504–10.
42. Hirabayashi Y, Shimizu R. Effect of age on extradural dose requirement in thoracic extradural anaesthesia. *Br J Anaesth*. 1993;71:445–6.

43. Perry F, Parker RK, White PF, Clifford PA. Role of psychological factors in postoperative pain control and recovery with patient-controlled analgesia. *Clin J Pain*. 1994;10:57–63.
44. Rhudy JL, Meagher MW. Fear and anxiety: divergent effects on human pain thresholds. *Pain*. 2000;84:65–75.
45. Bachiocco V, Morselli-Labate AM, Rusticali AG, Bragaglia R, Mastorilli M, Carli G. Intensity, latency and duration of post-thoracotomy pain: relationship to personality traits. *Funct Neurol*. 1990;5:321–32.
46. Caumo W, Schmidt AP, Schneider CN, et al. Preoperative predictors of moderate to intense acute postoperative pain in patients undergoing abdominal surgery. *Acta Anaesthesiol Scand*. 2002;46:1265–71.
47. Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. *Pain*. 2001;90:261–9.
48. Tasmuth T, Estlander AM, Kalso E. Effect of present pain and mood on the memory of past postoperative pain in women treated surgically for breast cancer. *Pain*. 1996;68:343–7.
49. Landreneau RJ, Hazelrigg SR, Mack MJ, et al. Postoperative pain-related morbidity: video-assisted thoracic surgery versus thoracotomy. *Ann Thorac Surg*. 1993;56:1285–9.
50. Iwasaki A, Hamatake D, Shirakusa T. Biosorbable poly-L-lactide rib-connecting pins may reduce acute pain after thoracotomy. *Thorac Cardiovasc Surg*. 2004;52:49–53.
51. Bethencourt DM, Holmes EC. Muscle-sparing posterolateral thoracotomy. *Ann Thorac Surg*. 1988;45:337–9.
52. Ginsberg RJ. Alternative (muscle-sparing) incisions in thoracic surgery. *Ann Thorac Surg*. 1993;56:752–4.
53. Fry WA. Thoracic incisions. *Chest Surg Clin N Am*. 1995;5:177–88.
54. Khan IH, McManus KG, McCraith A, McGuigan JA. Muscle sparing thoracotomy: a biomechanical analysis confirms preservation of muscle strength but no improvement in wound discomfort. *Eur J Cardiothorac Surg*. 2000;18:656–61.
55. Ochroch EA, Gottschalk A, Augoustides JG, et al. Pain and physical function are similar following axillary, muscle-sparing vs posterolateral thoracotomy. *Chest*. 2005;128:2664–70.
56. Benedetti F, Vighetti S, Ricco C, et al. Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. *J Thorac Cardiovasc Surg*. 1998;115:841–7.
57. Macchiarini P, Ladurie FL, Cerrina J, et al. Clamshell or sternotomy for double lung or heart-lung transplantation? *Eur J Cardiothorac Surg*. 1999;15:333–9.
58. Boulanger A, Choinière M, Roy D, et al. Comparison between patient-controlled analgesia and intramuscular meperidine after thoracotomy. *Can J Anaesth*. 1993;40:409–15.
59. Ballantyne JC, Carr DB, Chalmers TC, et al. Postoperative patient-controlled analgesia: meta-analyses of initial randomized control trials. *J Clin Anesth*. 1993;5:182–93.
60. Bullingham RES. Optimum management of postoperative pain. *Drugs*. 1985;29:376–86.
61. Bullingham RES. Postoperative pain. *Postgrad Med J*. 1984;60: 847–51.
62. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86:598–612.
63. Guignard B, Bossard AE, Coste C, et al. Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requirement. *Anesthesiology*. 2000;93:409–17.
64. Rømsing J, Møiniche S, Østergaard D, Dahl JB. Local infiltration with NSAIDs for postoperative analgesia: evidence for a peripheral analgesic action. *Acta Anaesthesiol Scand*. 2000;44:672–83.
65. Bjørkman R, Hedner T, Hallman KM, Henning M, Hedner J. Localisation of the central antinociceptive effects of diclofenac in the rat. *Brain Res*. 1992;590:66–73.
66. Vanegas H, Schaible HG. Prostaglandins and cyclooxygenases [correction of cycloxygenases] in the spinal cord. *Prog Neurobiol*. 2001;64:327–63.
67. Hawkey CJ. Non-steroidal anti-inflammatory drugs and peptic ulcers. *BMJ*. 1990;300:278–84.
68. Souter AJ, Fredman B, White PF. Controversies in the perioperative use of nonsteroidal antiinflammatory drugs. *Anesth Analg*. 1994;79:1178–90.
69. Møiniche S, Rømsing J, Dahl JB, Tramèr MR. Nonsteroidal antiinflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. *Anesth Analg*. 2003;96:68–77.
70. Appadurai IR, Power I. NSAIDS in the postoperative period. Use with caution in elderly people. *BMJ*. 1993;307:257.
71. Gibson P, Weadington D, Winney RJ. NSAIDS in the postoperative period. Clinical experience confirms risk. *BMJ*. 1993;307:257–8.
72. Keenan DJ, Cave K, Langdon L, Lea RE. Comparative trial of rectal indomethacin and cryoanalgesia for control of early post-thoracotomy pain. *BMJ*. 1983;287:1335–7.
73. Pavly T, Medley C, Murphy DF. Effect of indomethacin on pain relief after thoracotomy. *Br J Anaesth*. 1990;65:624–7.
74. Rhodes M, Conacher I, Morritt G, Hilton C. Nonsteroidal anti-inflammatory drugs for postthoracotomy pain. A prospective controlled trial after lateral thoracotomy. *J Thorac Cardiovasc Surg*. 1992;103:17–20.
75. Bigler D, Moller J, Kamp-Jensen M, Berthelsen P, Hjortso NC, Kehlet H. Effect of piroxicam in addition to continuous thoracic epidural bupivacaine and morphine on postoperative pain and lung function after thoracotomy. *Acta Anaesthesiol Scand*. 1992;36:647–50.
76. Barak M, Ziser A, Katz Y. Thoracic epidural local anesthetics are ineffective in alleviating post-thoracotomy ipsilateral shoulder pain. *J Cardiothorac Vasc Anesth*. 2004;18:458–60.
77. Goppelt-Strubbe M. Regulation of prostaglandin endoperoxide synthase (cyclooxygenase) isoenzyme expression. *Prostaglandins Leukot Essent Fatty Acids*. 1995;52:213–22.
78. Tröster A, Sittl R, Singler B, Schmelz M, Schüttler J, Koppert W. Modulation of remifentanil-induced analgesia and postinfusion hyperalgesia by parecoxib in humans. *Anesthesiology*. 2006;105:1016–23.
79. Einhorn TA. Cox-2: where are we in 2003? – The role of cyclooxygenase-2 in bone repair. *Arthritis Res Ther*. 2003;5: 5–7.
80. Glassman SD, Rose SM, Dimar JR, Puno RM, Campbell MJ, Johnson JR. The effect of postoperative nonsteroidal anti-inflammatory drug administration on spinal fusion. *Spine*. 1998; 23:834–8.
81. Graham DJ, Campen D, Hui R, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study. *Lancet*. 2005;365:475–81.

82. Hippisley-Cox J, Coupland C. Risk of myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. *BMJ*. 2005;330:1366.
83. Ott E, Nussmeier NA, Duke PC, et al. Efficacy and safety of the cyclooxygenase 2 inhibitors parecoxib and valdecoxib in patients undergoing coronary artery bypass surgery. *J Thorac Cardiovasc Surg*. 2003;125:1481–92.
84. Nussmeier NA, Whelton AA, Brown MT, et al. Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery. *N Engl J Med*. 2005;352:1081–91.
85. Nussmeier NA, Whelton AA, Brown MT, et al. Safety and efficacy of the cyclooxygenase-2 inhibitors parecoxib and valdecoxib after noncardiac surgery. *Anesthesiology*. 2006;104:518–26.
86. Joshi GP, Gertler R, Fricker R. Cardiovascular thromboembolic adverse effects associated with cyclooxygenase-2 selective inhibitors and nonselective antiinflammatory drugs. *Anesth Analg*. 2007;105:1793–804.
87. Flower RJ, Vane JR. Inhibition of prostaglandin synthetase in brain explains the anti-pyretic activity of paracetamol (4-acetaminophenol). *Nature*. 1972;240:410–1.
88. Tjølsen A, Lund A, Hole K. Antinociceptive effect of paracetamol in rats is partly dependent on spinal serotonergic systems. *Eur J Pharmacol*. 1991;193:193–201.
89. Honoré P, Buritova J, Besson JM. Aspirin and acetaminophen reduced both Fos expression in rat lumbar spinal cord and inflammatory signs produced by carrageenin inflammation. *Pain*. 1995;63:365–75.
90. Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. *Br J Anaesth*. 2005;94:505–13.
91. Montgomery JE, Sutherland CJ, Kestin IG, Sneyd JR. Morphine consumption in patients receiving rectal paracetamol and diclofenac alone and in combination. *Br J Anaesth*. 1996;77:445–7.
92. Seymour RA, Kelly PJ, Hawkesford JE. The efficacy of ketoprofen and paracetamol (acetaminophen) in postoperative pain after third molar surgery. *Br J Clin Pharmacol*. 1996;41:581–5.
93. Mac TB, Girard F, Chouinard P, et al. Acetaminophen decreases early post-thoracotomy ipsilateral shoulder pain in patients with thoracic epidural analgesia: a double-blind placebo-controlled study. *J Cardiothorac Vasc Anesth*. 2005;19:475–8.
94. Dahl V, Ræder JC. Non-opioid postoperative analgesia. *Acta Anaesthesiol Scand*. 2000;44:1191–203.
95. Hernández-Palazón J, Tortosa JA, Martínez-Lage JF, Pérez-Flores D. Intravenous administration of propacetamol reduces morphine consumption after spinal fusion surgery. *Anesth Analg*. 2001;92:1473–6.
96. Cattabriga I, Pacini D, Lamazza G, et al. Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial. *Eur J Cardiothorac Surg*. 2007;32:527–31.
97. Lahtinen P, Kokki H, Hendolin H, Hakala T, Hyyninen M. Propacetamol as adjunctive treatment for postoperative pain after cardiac surgery. *Anesth Analg*. 2002;95:813–9.
98. Mao J, Price DD, Mayer DJ. Mechanisms of hyperalgesia and morphine tolerance: a current view of their possible interactions. *Pain*. 1995;62:259–74.
99. Célèrier E, Rivat C, Jun Y, et al. Long-lasting hyperalgesia induced by fentanyl in rats: preventive effect of ketamine. *Anesthesiology*. 2000;92:465–72.
100. Guillou N, Tanguy M, Seguin P, Branger B, Campion JP, Mallédant Y. The effects of small-dose ketamine on morphine consumption in surgical intensive care unit patients after major abdominal surgery. *Anesth Analg*. 2003;97:843–7.
101. Michelet P, Guerville C, Hélaine A, et al. Adding ketamine to morphine for patient-controlled analgesia after thoracic surgery: influence on morphine consumption, respiratory function, and nocturnal desaturation. *Br J Anaesth*. 2007;99:396–403.
102. Suzuki M, Haraguti S, Sugimoto K, Kikutani T, Shimada Y, Sakamoto A. Low-dose intravenous ketamine potentiates epidural analgesia after thoracotomy. *Anesthesiology*. 2006;105:111–9.
103. Serpell MG. Gabapentin in neuropathic pain syndromes: a randomised, double-blind, placebo-controlled trial. *Pain*. 2002;99:557–66.
104. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus Muller L. Gabapentin for the treatment of postherpetic neuralgia. *JAMA*. 1998;280:1837–42.
105. Maneuf YP, Gonzalez MI, Sutton KS, Chung FZ, Pinnock RD, Lee K. Cellular and molecular action of the putative GABA-mimetic, gabapentin. *Cell Mol Life Sci*. 2003;60:742–50.
106. Kong VK, Irwin MG. Gabapentin: a multimodal perioperative drug? *Br J Anaesth*. 2007;99:775–86.
107. Mathiesen O, Møiniche S, Dahl JB. Gabapentin and postoperative pain: a qualitative and quantitative systematic review, with focus on procedure. *BMC Anesthesiol*. 2007;7:6.
108. Ménigaux C, Adam F, Guignard B, Sessler DI, Chauvin M. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. *Anesth Analg*. 2005;100:1394–9.
109. Huot MP, Chouinard P, Girard F, Ruel M, Lafontaine ER, Ferraro P. Gabapentin does not reduce post-thoracotomy shoulder pain: a randomized, double-blind placebo-controlled study. *Can J Anaesth*. 2008;55:337–43.
110. Jokela RM, Ahonen JV, Tallgren MK, Marjakangas PC, Korttila KT. The effective analgesic dose of dexamethasone after laparoscopic hysterectomy. *Anesth Analg*. 2009;109:607–15.
111. Kardash KJ, Sarrazin F, Tessler MJ, Velly AM. Single-dose dexamethasone reduces dynamic pain after total hip arthroplasty. *Anesth Analg*. 2008;106:1253–7.
112. Hval K, Thagaard KS, Schlichting E, Raeder J. The prolonged postoperative analgesic effect when dexamethasone is added to a nonsteroidal antiinflammatory drug (rofecoxib) before breast surgery. *Anesth Analg*. 2007;105:481–6.
113. Bisgaard T, Klarskov B, Kehlet H, Rosenberg J. Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. *Ann Surg*. 2003;238:651–60.
114. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150:971–9.
115. Carroll D, Tramèr M, McQuay H, Nye B, Moore A. Randomization is important in studies with pain outcomes: systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. *Br J Anaesth*. 1996;77:798–803.
116. Stratton SA, Smith MM. Postoperative thoracotomy. Effect of transcutaneous electrical nerve stimulation on forced vital capacity. *Phys Ther*. 1980;60:45–7.

117. Rooney SM, Jain S, Goldiner PL. Effect of transcutaneous nerve stimulation on postoperative pain after thoracotomy. *Anesth Analg*. 1983;62:1010–2.
118. Warfield CA, Stein JM, Frank HA. The effect of transcutaneous electrical nerve stimulation on pain after thoracotomy. *Ann Thorac Surg*. 1985;39:462–5.
119. Stubbing JF, Jellicoe JA. Transcutaneous electrical nerve stimulation after thoracotomy. Pain relief and peak expiratory flow rate – a trial of transcutaneous electrical nerve stimulation. *Anaesthesia*. 1988;43:296–8.
120. Benedetti F, Amanzio M, Casadio C, et al. Control of postoperative pain by transcutaneous electrical nerve stimulation after thoracic operations. *Ann Thorac Surg*. 1997;63:773–6.
121. Erdogan M, Erdogan A, Erbil N, Karakaya HK, Demircan A. Prospective, randomized, placebo-controlled study of the effect of TENS on postthoracotomy pain and pulmonary function. *World J Surg*. 2005;29:1563–70.
122. Solak O, Turna A, Pekcolaklar A, et al. Transcutaneous electric nerve stimulation for the treatment of postthoracotomy pain: a randomized prospective study. *Thorac Cardiovasc Surg*. 2007;55:182–5.
123. Gough JD, Williams AB, Vaughan RS, Khalil JF, Butchart EG. The control of post-thoracotomy pain. A comparative evaluation of thoracic epidural fentanyl infusions and cryo-analgesia. *Anaesthesia*. 1988;43:780–3.
124. Muller LC, Salzer GM, Ransmayer G, Neiss A. Intraoperative cryoanalgesia for postthoracotomy pain relief. *Ann Thorac Surg*. 1989;48:15–8.
125. Liu SS, Richman JM, Thirlby RC, Wu CL. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. *J Am Coll Surg*. 2006;203:914–32.
126. Hahnenkamp K, Theilmeier G, Van Aken HK, Hoenemann CW. The effects of local anesthetics on perioperative coagulation, inflammation, and microcirculation. *Anesth Analg*. 2002;94:1441–7.
127. Hardy PA. Anatomical variation in the position of the proximal intercostal nerve. *Br J Anaesth*. 1988;61:338–9.
128. Dryden CM, McMenemin I, Duthie DJ. Efficacy of continuous intercostal bupivacaine for pain relief after thoracotomy. *Br J Anaesth*. 1993;70:508–10.
129. Chan VW, Chung F, Cheng DC, Seyone C, Chung A, Kirby TJ. Analgesic and pulmonary effects of continuous intercostal nerve block following thoracotomy. *Can J Anaesth*. 1991;38:733–9.
130. Bachmann-Mennenga B, Biscoping J, Kuhn DF, et al. Intercostal nerve block, interpleural analgesia, thoracic epidural block or systemic opioid application for pain relief after thoracotomy? *Eur J Cardiothorac Surg*. 1993;7:12–8.
131. Dravid RM, Paul RE. Interpleural block – Part 1. *Anaesthesia*. 2007;62:1039–49.
132. Kvalheim L, Reiestad F. Intrapleural catheter in the management of postoperative pain. *Anesthesiology*. 1984;61:A231.
133. Miguel R, Smith R. Intrapleural, not interpleural, analgesia. *Reg Anesth*. 1991;16:299.
134. Baumgarten RK. Intrapleural, interpleural, or pleural block? Simpler may be better. *Reg Anesth*. 1992;17:116.
135. Murphy DF. Interpleural analgesia. *Br J Anaesth*. 1993;71:426–34.
136. Schneider RF, Villamena PC, Harvey J, Surick BG, Surick IW, Beattie EJ. Lack of efficacy of intrapleural bupivacaine for postoperative analgesia following thoracotomy. *Chest*. 1993;103:414–6.
137. Miguel R, Hubbell D. Pain management and spirometry following thoracotomy: a prospective, randomized study of four techniques. *J Cardiothorac Vasc Anesth*. 1993;7:529–34.
138. Raffin L, Fletcher D, Sperandio M, et al. Interpleural infusion of 2% lidocaine with 1:200,000 epinephrine for postthoracotomy analgesia. *Anesth Analg*. 1994;79:328–34.
139. Rosenberg PH, Scheinin BM, Lepantalo MJ, Lindfors O. Continuous intrapleural infusion of bupivacaine for analgesia after thoracotomy. *Anesthesiology*. 1987;67:811–3.
140. Kambam JR, Hammon J, Parris WC, Lupinetti FM. Intrapleural analgesia for post-thoracotomy pain and blood levels of bupivacaine following intrapleural injection. *Can J Anaesth*. 1989;36:106–9.
141. Broome IJ, Sherry KM, Reilly CS. A combined chest drain and intrapleural catheter for post-thoracotomy pain relief. *Anesthesia*. 1993;48:724–6.
142. Pennefather SH, Akrofi ME, Kendall JB, Russell GN, Scawn ND. Double-blind comparison of intrapleural saline and 0.25% bupivacaine for ipsilateral shoulder pain after thoracotomy in patients receiving thoracic epidural analgesia. *Br J Anaesth*. 2005;94:234–8.
143. Sellheim H. Verh Dtch Ges Gynak. 1906;176.
144. Eason MJ, Wyatt R. Paravertebral thoracic block-a reappraisal. *Anesthesia*. 1979;34:638–42.
145. Lönnqvist PA, Hildingsson U. The caudal boundary of the thoracic paravertebral space. A study in human cadavers. *Anesthesia*. 1992;47:1051–2.
146. Karmakar MK. Thoracic paravertebral block. *Anesthesiology*. 2001;95:771–80.
147. Nunn JF, Slavin G. Posterior intercostal nerve block for pain relief after cholecystectomy. Anatomical basis and efficacy. *Br J Anaesth*. 1980;52:253–60.
148. Curley J, Castillo J, Hotz J, et al. Prolonged regional nerve blockade. Injectable biodegradable bupivacaine/polyester microspheres. *Anesthesiology*. 1996;84:1401–10.
149. Castillo J, Curley J, Hotz J, et al. Glucocorticoids prolong rat sciatic nerve blockade in vivo from bupivacaine microspheres. *Anesthesiology*. 1996;85:1157–66.
150. Drager C, Benziger D, Gao F, Berde C. Prolonged intercostal nerve blockade in sheep using controlled-release of bupivacaine and dexamethasone from polymer microspheres. *Anesthesiology*. 1998;89:969–79.
151. Kopacz DJ, Lacouture PG, Wu D, Nandy P, Swanton R, Landau C. The dose response and effects of dexamethasone on bupivacaine microcapsules for intercostal blockade (T9 to T11) in healthy volunteers. *Anesth Analg*. 2003;96:576–82.
152. Grant GJ, Vermeulen K, Langerman L, Zakowski M, Turndorf H. Prolonged analgesia with liposomal bupivacaine in a mouse model. *Reg Anesth*. 1994;19:264–9.
153. Grant GJ, Lax J, Susser L, Zakowski M, Weissman TE, Turndorf H. Wound infiltration with liposomal bupivacaine prolongs analgesia in rats. *Acta Anaesthesiol Scand*. 1997;4:204–7.
154. Boogaerts JG, Lafont ND, Declercq AG, et al. Epidural administration of liposome-associated bupivacaine for the management of postsurgical pain: a first study. *J Clin Anesth*. 1994;6:315–20.
155. Wang CF, Djalali AG, Gandhi A, et al. An absorbable local anesthetic matrix provides several days of functional sciatic nerve blockade. *Anesth Analg*. 2009;108:1027–33.

156. Burns DA, Ben-David B, Chelly JE, Greensmith JE. Inter-costally placed paravertebral catheterization: an alternative approach to continuous paravertebral blockade. *Anesth Analg.* 2008;107:339–41.
157. Sabanathan S, Smith PJ, Pradhan GN, Hashimi H, Eng JB, Mearns AJ. Continuous intercostal nerve block for pain relief after thoracotomy. *Ann Thorac Surg.* 1988;46:425–6.
158. Berrisford RG, Sabanathan SS. Direct access to the paravertebral space at thoracotomy. *Ann Thorac Surg.* 1990;49:854.
159. Soni AK, Conacher I, Waller DA, Hilton CJ. Video-assisted thoracoscopic placement of paravertebral catheters. *Br J Anaesth.* 1994;72:462–4.
160. Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and metaregression. *Br J Anaesth.* 2009;103:626–36.
161. Berrisford RG, Sabanathan S, Mearns AJ, Clarke BJ, Hamdi A. Plasma concentrations of bupivacaine and its enantiomers during continuous extrapleural intercostal nerve block. *Br J Anaesth.* 1993;70:201–4.
162. Richardson J, Sabanathan S, Jones J, Shah RD, Cheema S, Mearns AJ. A prospective, randomized comparison of preoperative and continuous balanced epidural or paravertebral bupivacaine on post-thoracotomy pain, pulmonary function and stress responses. *Br J Anaesth.* 1999;83:387–92.
163. Association of Anaesthetists of Great Britain and Ireland. Guidelines for the management of severe local anaesthetic toxicity. August 2009. <http://www.aagbi.org/publications/guidelines/docs/latoxicity07.pdf>. Accessed 20 Oct 2009.
164. Resuscitation Council (UK) website. September 2009. <http://www.resus.org.uk/pages/caLocalA.html>. Accessed 4 July 2009.
165. Samii K, Feret J, Harari A, Viars P. Selective spinal analgesia. *Lancet.* 1979;1:1142.
166. Mason N, Gondret R, Junca A, Bonnet F. Intrathecal sufentanil and morphine for post-thoracotomy pain relief. *Br J Anaesth.* 2001;86:236–40.
167. Liu N, Kuhlman G, Dalibon N, Moutafis M, Levron JC, Fischler M. A randomized, double-blinded comparison of intrathecal morphine, sufentanil and their combination versus IV morphine patient-controlled analgesia for postthoracotomy pain. *Anesth Analg.* 2001;92:31–6.
168. Neustein SM, Cohen E. Intrathecal morphine during thoracotomy, Part II: effect on postoperative meperidine requirements and pulmonary function tests. *J Cardiothorac Vasc Anesth.* 1993;7:157–9.
169. Liu M, Rock LM, Grass JA, et al. Double-blind randomized evaluation of intercostal nerve blocks as an adjuvant to subarachnoid administered morphine for post-thoracotomy analgesia. *Reg Anesth.* 1995;20:418–25.
170. Sudarshan G, Browne B, Matthews J, Conacher I. Intrathecal fentanyl for post-thoracotomy pain. *Br J Anaesth.* 1995;75: 19–22.
171. Gray JR, Fromme GA, Nauss LA, Wang JK, Ilstrup DM. Intrathecal morphine for postthoracotomy pain. *Anesth Analg.* 1986;65:873–6.
172. Cohen E, Neustein SM. Intrathecal morphine during thoracotomy, Part I: effect on intraoperative enflurane requirements. *J Cardiothorac Vasc Anesth.* 1993;7:154–6.
173. Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. *Anesthesiology.* 1984;61:276–310.
174. Ng A, Swanevelder J. Pain relief after thoracotomy: is epidural analgesia the optimal technique? *Br J Anaesth.* 2007;98:159–62.
175. Sicard A. Les injections medicamenteuses extra-durales par voie sacrococcygienne. *Compt Rend Soc De Biol.* 1901;53: 396–8.
176. Pagés F. Anesthesia metamerica. *Rev Esp Chir.* 1921;3:3–30.
177. Dogliotti AM. A new method of block: segmental peridural spinal anesthesia. *Am J Surg.* 1933;20:107–18.
178. Logas WG, el-Baz N, el-Ganzouri A, et al. Continuous thoracic epidural analgesia for postoperative pain relief following thoracotomy: a randomized prospective study. *Anesthesiology.* 1987;67:787–91.
179. Muneyuki M, Shirai K, Inamoto A. Roentgenographic analysis of the positions of catheters in the epidural space. *Anesthesiology.* 1970;33:19–24.
180. Motamed C, Farhat F, Rémérand F, Stéphanazzi J, Laplanche A, Jayr C. An analysis of postoperative epidural analgesia failure by computed tomography epidurography. *Anesth Analg.* 2006;103:1026–32.
181. Königsrainer I, Bredanger S, Drewel-Frohnmeier R, et al. Audit of motor weakness and premature catheter dislodgement after epidural analgesia in major abdominal surgery. *Anesthesia.* 2009;64:27–31.
182. Conacher ID, Paes ML, Jacobson L, Phillips PD, Heaviside DW. Epidural analgesia following thoracic surgery. *Anesthesia.* 1983;38:546–51.
183. Kaneko M, Saito Y, Kirihara Y, Collins JG, Kosaka Y. Synergistic antinociceptive interaction after epidural coadministration of morphine and lidocaine in rats. *Anesthesiology.* 1994;80: 137–50.
184. Curatolo M, Schnider TW, Petersen-Felix S, et al. A direct search procedure to optimize combinations of epidural bupivacaine, fentanyl, and clonidine for postoperative analgesia. *Anesthesiology.* 2000;92:325–37.
185. Mahon SV, Berry PD, Jackson M, Russell GN, Pennefather SH. Thoracic epidural infusions for post-thoracotomy pain: are fentanyl-bupivacaine mixtures better than fentanyl alone? *Anesthesia.* 1999;54:641–6.
186. Tan CNH, Guha A, Scawn NDA, Pennefather SH, Russell GN. Optimal concentration of epidural fentanyl in bupivacaine 0.1% after thoracotomy. *Br J Anaesth.* 2004;92:670–4.
187. Niemi G, Breivik H. Epinephrine markedly improves thoracic epidural analgesia produced by a small-dose infusion of ropivacaine, fentanyl, and epinephrine after major thoracic or abdominal surgery: a randomized, double-blinded crossover study with and without epinephrine. *Anesth Analg.* 2002;94:1598–605.
188. Eisenach JC, De Kock M, Klimscha W. alpha(2)-Adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984–1995). *Anesthesiology.* 1996;85:655–74.
189. Visser WA, Liem TH, van Egmond J, Gielen MJ. Extension of sensory blockade after thoracic epidural administration of a test dose of lidocaine at three different levels. *Anesth Analg.* 1998;86:332–5.
190. Lee CJ, Jeon Y, Lim YJ, et al. The influence of neck flexion and extension on the distribution of contrast medium in the high thoracic epidural space. *Anesth Analg.* 2007;104:1583–6.
191. Fratacci MD, Kimball WR, Wain JC, Kacmarek RM, Polaner DM, Zapol WM. Diaphragmatic shortening after thoracic surgery in humans. Effects of mechanical ventilation and thoracic epidural anesthesia. *Anesthesiology.* 1993;79:654–65.

192. Simonneau G, Vivien A, Sartene R, et al. Diaphragm dysfunction induced by upper abdominal surgery. Role of postoperative pain. *Am Rev Respir Dis.* 1983;128:899–903.
193. Dureuil B, Viires N, Cantineau JP, Aubier M, Desmonts JM. Diaphragmatic contractility after upper abdominal surgery. *J Appl Physiol.* 1986;61:1775–80.
194. Torres A, Kimball WR, Qvist J, et al. Sonomicrometric regional diaphragmatic shortening in awake sheep after thoracic surgery. *J Appl Physiol.* 1989;67:2357–68.
195. Polaner DM, Kimball WR, Fratacci MD, Wain JC, Zapol WM. Thoracic epidural anesthesia increases diaphragmatic shortening after thoracotomy in the awake lamb. *Anesthesiology.* 1993;79:808–16.
196. Manikian B, Cantineau JP, Bertrand M, Kieffer E, Sartene R, Viars P. Improvement of diaphragmatic function by a thoracic extradural block after upper abdominal surgery. *Anesthesiology.* 1988;68:379–86.
197. Warner DO, Warner MA, Ritman EL. Human chest wall function during epidural anesthesia. *Anesthesiology.* 1996;85:761–73.
198. Richter A, Cederholm I, Jonasson L, Mucchiano C, Uchto M, Janerot-Sjoberg B. Effect of thoracic epidural analgesia on refractory angina pectoris: long-term home self-treatment. *J Cardiothorac Vasc Anesth.* 2002;16:679–84.
199. Gramling-Babb P, Miller MJ, Reeves ST, Roy RC, Zile MR. Treatment of medically and surgically refractory angina pectoris with high thoracic epidural analgesia: initial clinical experience. *Am Heart J.* 1997;133:648–55.
200. Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. *Anesth Analg.* 2001;93:853–8.
201. Oka T, Ozawa Y, Ohkubo Y. Thoracic epidural bupivacaine attenuates supraventricular tachyarrhythmias after pulmonary resection. *Anesth Analg.* 2001;93:253–9.
202. Oka T, Ozawa Y. Correlation between intraoperative hemodynamic variability and postoperative arrhythmias in patients with pulmonary surgery. *Masui.* 1999;48:118–23.
203. Ritchie AJ, Bowe P, Gibbons JR. Prophylactic digitalization for thoracotomy: a reassessment. *Ann Thorac Surg.* 1990;50:86–8.
204. Krowka MJ, Pairolo PC, Trastek VF, et al. Cardiac dysrhythmia following pneumonectomy: clinical correlates and prognostic significance. *Chest.* 1987;91:490–5.
205. Von Knorring J, Lepantalo M, Lindgren L, Lindfors O. Cardiac arrhythmias and myocardial ischemia after thoracotomy for lung cancer. *Ann Thorac Surg.* 1992;53:642–7.
206. Modig J, Borg T, Karlstrom G, Maripuu E, Sahlstedt B. Thromboembolism after total hip replacement: role of epidural and general anesthesia. *Anesth Analg.* 1983;62:174–80.
207. Sharrock NE, Cazan MG, Hargett MJ, Williams-Russo P, Wilson Jr PD. Changes in mortality after total hip and knee arthroplasty over a ten-year period. *Anesth Analg.* 1995;80:242–8.
208. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ.* 2000;321:1493–7.
209. Rigg JR, Jamrozik K, Myles PS, Silbert BS, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet.* 2002;59:276–82.
210. Giebler RM, Scherer RU, Peters J. Incidence of neurologic complications related to thoracic epidural catheterization. *Anesthesiology.* 1997;86:55–63.
211. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. *Br J Anaesth.* 2001;87:47–61.
212. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *Br J Anaesth.* 1982;54:479–86.
213. Liu SS, Allen HW, Olsson GL. Patient-controlled epidural analgesia with bupivacaine and fentanyl on hospital wards: prospective experience with 1,030 surgical patients. *Anesthesiology.* 1998;88:688–95.
214. Shanker KB, Palkar NV, Nishkala R. Paraplegia following epidural potassium chloride. *Anesthesia.* 1985;40:45–7.
215. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. *Anesthesiology.* 2004;101:1950–9.
216. Gogarten W, Van Aken H, Riess H. German guidelines on regional anaesthesia and thromboembolism prophylaxis. *Anaesthesiologie und Intensivmedizin.* 2007;48:124–9.
217. Horlocker TT, Wedel DJ. Neurological complications of spinal and epidural anesthesia. *Reg Anesth Pain Med.* 2000;25:83–98.
218. Stafford-Smith M. Impaired haemostasis and regional anaesthesia. *Can J Anaesth.* 1996;43:R129–35.
219. Meikle J, Bird S, Nightingale J, White N. Detection and management of epidural haematomas related to anaesthesia in the UK: a national survey of current practice. *Br J Anaesth.* 2008;101:400–4.
220. CLASP (Collaborative Low-Dose Aspirin Study in Pregnancy) Collaborative Group. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. *Lancet.* 1994;343:619–29.
221. Horlocker TT, Bajwa ZH, Ashraft Z, et al. Risk assessment of hemorrhagic complications associated with nonsteroidal anti-inflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. *Anesth Analg.* 2002;95:1691–7.
222. Newsome LT, Kutcher MA, Royster RL. Coronary artery stents: Part I. Evolution of percutaneous coronary intervention. *Anesth Analg.* 2008;107:552–69.
223. Collins R, Scrimgeour A, Yusuf S, et al. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic and urologic surgery. *N Engl J Med.* 1988;318:1162–73.
224. Vandermeulen EP, Van Aken H, Vermeylen J. Anticoagulants and spinal-epidural anesthesia. *Anesth Analg.* 1994;79:1165–77.
225. Greaves JD. Serious spinal cord injury due to haematomyelia caused by spinal anesthesia in a patient treated with low dose heparin. *Anaesthesia.* 1997;52:150–4.
226. Sandhu H, Morley-Forster P, Spadafora S. Epidural hematoma following epidural analgesia in a patient receiving unfractionated heparin for thromboprophylaxis. *Reg Anesth Pain Med.* 2000;25:72–5.
227. Liu SS, Mulroy MF. Neuraxial anesthesia and analgesia in the presence of standard heparin. *Reg Anesth Pain Med.* 1998;23:157–63.
228. Bergqvist D, Lindblad B, Matzsch T. Low molecular weight heparin for thromboprophylaxis and epidural/spinal anaesthesia – is there a risk? *Acta Anaesthesiol Scand.* 1992;36:605–9.
229. Tryba M, Wedel DJ. Central neuraxial block and low molecular weight heparin (enoxaparin): lessons learned from two different dosage regimes in two continents. *Acta Anaesthesiol Scand.* 1997;41:100–4.

230. Bromage PR, Camporesi EM, Durant PA, Nielsen CH. Non-respiratory side effects of epidural morphine. *Anesth Analg*. 1982;61:490–5.
231. Yaksh TL. Spinal opiate analgesia: characteristics and principles of action. *Pain*. 1981;11:293–346.
232. Rawal N, Mollefors K, Axelsson K, Lingardh G, Widman B. An experimental study of urodynamic effects of epidural morphine and of naloxone reversal. *Anesth Analg*. 1983;62:641–7.
233. Husted S, Djurhuus JC, Husegaard HC, Jepsen J, Mortensen J. Effect of postoperative extradural morphine on lower urinary tract function. *Acta Anaesthesiol Scand*. 1985;29:183–5.
234. Wang J, Pennefather S, Russell G. Low-dose naloxone in the treatment of urinary retention during extradural fentanyl causes excessive reversal of analgesia. *Br J Anaesth*. 1998;80:565–6.
235. Goldhill DR, Whelpton R, Winyard JA, Wilkinson KA. Gastric emptying in patients the day after cardiac surgery. *Anaesthesia*. 1995;50:122–5.
236. Petring OU, Dawson PJ, Blake DW, et al. Normal postoperative gastric emptying after orthopaedic surgery with spinal anaesthesia and i.m. ketorolac as the first postoperative analgesic. *Br J Anaesth*. 1995;74:257–60.
237. Thorn SE, Wattwil M, Naslund I. Postoperative epidural morphine, but not epidural bupivacaine, delays gastric emptying on the first day after cholecystectomy. *Reg Anesth*. 1992;17:91–4.
238. Bonica JJ. Autonomic innervation of the viscera in relation to nerve block. *Anesthesiology*. 1968;29:793–813.
239. Guha A, Scawn NDA, Rogers SA, Pennefather SH, Russell GN. Gastric emptying in post thoracotomy patients receiving a thoracic fentanyl – bupivacaine epidural infusion. *Eur J Anaesthesiol*. 2002;19:652–7.
240. Lundberg JF, Martner J, Raner C. Dopamine or norepinephrine infusion during thoracic epidural anesthesia? Differences in hemodynamic effects and plasma catecholamine levels. *Acta Anaesthesiol Scand*. 2005;49:962–8.
241. Tan N, Agnew NM, Scawn ND, Pennefather SH, Chester M, Russell GN. Suprascapular nerve block for ipsilateral shoulder pain after thoracotomy with thoracic epidural analgesia: a double-blind comparison of 0.5% bupivacaine and 0.9% saline. *Anesth Analg*. 2002;94:199–202.
242. Danelli G, Berti M, Casati A, et al. Ipsilateral shoulder pain after thoracotomy surgery: a prospective, randomized, double-blind, placebo-controlled evaluation of the efficacy of infiltrating the phrenic nerve with 0.2%wt/vol ropivacaine. *Eur J Anaesthesiol*. 2007;24:596–601.
243. Ng KP, Chow YF. Brachial plexus block for ipsilateral shoulder pain after thoracotomy. *Anaesth Intensive Care*. 1997;25:74–6.
244. Barak M, Iaroshevski D, Poppa E, Ben-Nun A, Katz Y. Low-volume interscalene brachial plexus block for post-thoracotomy shoulder pain. *J Cardiothorac Vasc Anesth*. 2007;21:554–7.
245. Urmey WF, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:352–7.
246. Garner L, Coats RR. Ipsilateral stellate ganglion block effective for treating shoulder pain after thoracotomy. *Anesth Analg*. 1994;78:1195–6.
247. Kocabas S, Yedicocuklu D, Yuksel E, Uysallar E, Askar F. Infiltration of the sternotomy wound and the mediastinal tube sites with 0.25% levobupivacaine as adjunctive treatment for postoperative pain after cardiac surgery. *Eur J Anaesthesiol*. 2008;25:842–9.
248. Magnano D, Montalbano R, Lamarra M, et al. Ineffectiveness of local wound anesthesia to reduce postoperative pain after median sternotomy. *J Card Surg*. 2005;20:314–8.
249. McDonald SB, Jacobsohn E, Kopacz DJ, et al. Parasternal block and local anesthetic infiltration with levobupivacaine after cardiac surgery with desflurane: the effect on postoperative pain, pulmonary function, and tracheal extubation times. *Anesth Analg*. 2005;100:25–32.
250. Zingg U, McQuinn A, DiValentino D, et al. Minimally invasive versus open esophagectomy for patients with esophageal cancer. *Ann Thorac Surg*. 2009;87:911–9.
251. Perttunen K, Nilsson E, Heinonen J, Hirvisalo EL, Salo JA, Kalso E. Extradural, paravertebral and intercostal nerve blocks for post-thoracotomy pain. *Br J Anaesth*. 1995;75:541–7.
252. Matthews PJ, Govenden V. Comparison of continuous paravertebral and extradural infusions of bupivacaine for pain relief after thoracotomy. *Br J Anaesth*. 1989;62:204–5.
253. Coe A, Sarginson R, Smith MW, Donnelly RJ, Russell GN. Pain following thoracotomy. A randomised, double-blind comparison of lumbar versus thoracic epidural fentanyl. *Anaesthesia*. 1991;46:918–21.
254. Haak-van der Lely F, van Kleef JW, Burn AG, Bovill JG. An intra-operative comparison of lumbar with thoracic epidural sufentanil for thoracotomy. *Anaesthesia*. 1994;49:119–21.
255. Thomson CA, Becker DR, Messick Jr JM, et al. Analgesia after thoracotomy: effects of epidural fentanyl concentration/infusion rate. *Anesth Analg*. 1995;81:973–81.
256. Licker MJ, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg*. 2006;81:1830–7.
257. Powell ES, Pearce AC, Cook D, et al. UK pneumonectomy outcome study (UKPOS): a prospective observational study of pneumonectomy outcome. *J Cardiothorac Surg*. 2009;4:41.
258. Cense HA, Lagarde SM, de Jong K, et al. Association of no epidural analgesia with postoperative morbidity and mortality after transthoracic esophageal cancer resection. *J Am Coll Surg*. 2006;202:395–400.
259. Smedstad KG, Beattie WS, Blair WS, Buckley DN. Postoperative pain relief and hospital stay after total esophagectomy. *Clin J Pain*. 1992;8:149–53.
260. Whooley BP, Law S, Murthy SC, Alexandrou A, Wong J. Analysis of reduced death and complication rates after esophageal resection. *Ann Surg*. 2001;233:338–44.
261. Watson A, Allen PR. Influence of thoracic epidural analgesia on outcome after resection for esophageal cancer. *Surgery*. 1994;115:429–32.
262. Law S, Wong KH, Kwok KF, et al. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. *Ann Surg*. 2004;240:791–800.
263. Michelet P, D'Journo XB, Roch A, et al. Perioperative risk factors for anastomotic leakage after esophagectomy: influence of thoracic epidural analgesia. *Chest*. 2005;128:3461–6.
264. Page RD, Shackcloth MJ, Russell GN, Pennefather SH. Surgical treatment of anastomotic leaks after oesophagectomy. *Eur J Cardiothorac Surg*. 2005;27:337–43.
265. Ikeda Y, Niimi M, Kan S, Shatari T, Takami H, Kodaira S. Clinical significance of tissue blood flow during esophagectomy by laser Doppler flowmetry. *J Thorac Cardiovasc Surg*. 2001;122:1101–6.

266. Al-Rawi OY, Pennefather SH, Page RD, Dave I, Russell GN. The effect of thoracic epidural bupivacaine and an intravenous adrenaline infusion on gastric tube blood flow during esophagectomy. *Anesth Analg.* 2008;106:884–7.
267. Michelet P, Roch A, D'Journo XB, et al. Effect of thoracic epidural analgesia on gastric blood flow after oesophagectomy. *Acta Anaesthesiol Scand.* 2007;51:587–94.
268. Kelly FE, Murdoch JA, Sanders DJ, Berrisford RG. Continuous paravertebral block for thoraco-abdominal oesophageal surgery. *Anaesthesia.* 2005;60:98–9.
269. de Leon-Casasola OA, Lema MJ. Epidural sufentanil for acute pain control in a patient with extreme opioid dependency. *Anesthesiology.* 1992;76:853–6.
270. de Leon-Casasola OA, Lema MJ. Epidural bupivacaine/sufentanil therapy for postoperative pain control in patients tolerant to opioid and unresponsive to epidural bupivacaine/morphine. *Anesthesiology.* 1994;80:303–9.
271. Rapp SE, Ready LB, Nessly ML. Acute pain management in patients with prior opioid consumption: a case-controlled retrospective review. *Pain.* 1995;61:195–201.
272. Swenson JD, Davis JJ, Johnson KB. Postoperative care of the chronic opioid-consuming patient. *Anesthesiol Clin North America.* 2005;23:37–48.
273. Fitzgibbon DR, Ready LB. Intravenous high-dose methadone administered by patient controlled analgesia and continuous infusion for the treatment of cancer pain refractory to high-dose morphine. *Pain.* 1997;73:259–61.
274. Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med.* 2004;29:576–91.
275. Barrington MJ, Scott DA. Do we need to justify epidural analgesia beyond pain relief? *Lancet.* 2008;372:514–6.
276. Landreneau RJ, Mack MJ, Hazelrigg SR, et al. Prevalence of chronic pain. *J Thorac Cardiovasc Surg.* 1994;107:1079–85.
277. Ramamurthy S. Thoracic epidural nerve block. In: Waldman SD, Winnie AP, editors. *Interventional pain management.* Philadelphia: WB Saunders; 1996.
278. Gosling JA, Harris PF, Humpherson JR. *Atlas of human anatomy.* London: Churchill Livingstone; 1985.
279. Pennefather SH, Russell GN. Postthoracotomy analgesia. In: Slinger PD, editor. *Progress in thoracic anaesthesia, A Society of Cardiovascular Anesthesiologist Monograph.* Philadelphia: Lippincott Williams & Wilkins; 2004.
280. Gottschalk A, Cohen SP, Yang S, Ochroch EA. Preventing and treating pain after thoracic surgery. *Anesthesiology.* 2006;104:594–600.

Prevention and Management of Chronic Post-Thoracotomy Pain

Peter MacDougall

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Key Points

- Chronic post-thoracotomy pain (CPTP) is a common side effect of thoracotomy affecting up to one half of patients.
- The prevalence and intensity of CPTP may gradually decrease over time.
- More than one half of CPTP is neuropathic in nature.
- CPTP has a profound impact on patient function. It impairs sleep and daily activity. Forty percent of patients continue to take analgesic medications more than 2 years after the surgery.
- Anterior axillary thoracotomy and anterior limited thoracotomy may provide better early post-operative pain control. Improved pain control extends to at least 6 months after surgery. Rates of CPTP after VATS surgery are not significantly different than those after standard thoracotomy techniques.
- Factors predicting CPTP include greater acute post-operative pain, younger age and emotional numbing. An inefficient diffuse noxious inhibitory control system (DNIC) may predict CPTP.
- It is unclear whether thoracic epidural analgesia or paravertebral blockade prevent CPTP. Studies to date have been few and may be underpowered.
- It is prudent to make all efforts to reduce acute pain after thoracotomy by employing a multi-modal analgesic strategy. CPTP may be managed based on published guidelines for management of neuropathic pain. Recurrence of malignancy should be excluded.

Introduction

The past two to three decades have heralded the realization that surgery represents more than an injury to the patient. As with many injuries, it has become increasingly clear that virtually all surgical procedures may be associated with a chronic pain state [1–6]. The incidence of chronic post-surgical pain (CPSP) among common procedures may be astonishingly high (Table 47.1) [2, 6]. Rates of CPSP ranging as high as 51% are common [2, 3, 6]. In addition, chronic pain after surgical procedures may range in intensity from minor to pain of severity such that it interferes with the persons' daily activity [2]. Pain that is significant enough to affect daily function may also affect the ability of the patient to return to normal function after surgery. These normal functions include returning to work, returning to normal duties in the home or even the ability to return to living independently.

While chronic pain after surgery has a profound impact on the life of the person affected, it will also secondarily affect family, friends and co-workers. The burden of caring for persons with chronic pain is enormous. Macrae [3] estimated that between 41,000 and 395,000 new cases of CPSP per year may be expected in the UK given the most recent data on surgical numbers. Data from the US as recently as 2006 indicates that amputation, breast cancer surgery, herniorrhaphy, caesarean section and coronary artery bypass surgery account for approximately 2.1 million surgical procedures [6]. Clearly, if even 5% of these persons required ongoing health care for treatment of the pain, the costs would soon become overwhelming.

TABLE 47.1. The incidence of chronic postsurgical pain (CPSP) among common procedures

Type of surgery	Incidence of chronic pain (%)
Mastectomy	20–50
Caesarean section	6
Amputation	50–85
Cardiac surgery	30–55
Hernia repair	5–35
Cholecystectomy	5–50
Hip replacement	12
Thoracotomy	5–65

Reproduced from McRae [3], with permission from Oxford University Press

Some of the most common CPSP syndromes are those reported after limb amputation, breast surgery, hernia repair and thoracotomy [2, 3]. Surgery for breast cancer has been reported to cause significant pain especially after mastectomy [2, 7–10], with rates of post-mastectomy pain ranging from approximately 20% to greater than 51% [8–10]. Pain after limb amputation was perhaps the first recognized postsurgical pain and is characterized by neuropathic pain and pain over the stump [11, 12]. Unfortunately, this pain is present in up to 81% of patients undergoing amputation of a limb [11–13]. Post-herniorrhaphy pain is perhaps one of the most studied forms of chronic pain. Moderate-to-severe pain has been reported in about 10% of patients having herniorrhaphy [14, 15]. Herniorrhaphy is an especially common surgery and 2–6% of patients having this procedure have long-term pain severe enough to interfere with daily activities [15]. This is of particular concern as this is a common procedure involving patients who are active in the workforce.

Chronic Post-Thoracotomy Pain

Invasion of the chest cavity by human hands is fraught with challenges both for the surgeon and the patient. In addition to the multitude of immediate physiologic perturbations described throughout this book, patients are at risk of developing a pain syndrome as a direct result of the surgery. This chapter discusses chronic post-thoracotomy pain (CPTP), the causes as they are known so far, prevention and management of this challenging entity and some of the challenges that the future holds.

Incidence and Time Course of Chronic Post-Thoracotomy Pain

Pain following thoracotomy has been described as one of the most intense post-operative forms of pain known. Acute post-operative pain has been demonstrated to interfere with a number of physiological parameters and considerable effort has been devoted to developing methods to ameliorate this pain. CPTP has been defined as pain that extends at least 2 months [2],

or 3 months after surgery [16]. Variability in this definition continues to exist in the literature, but it is generally accepted that by 3 months after surgery, pain that remains represents a chronic state.

The pain of CPTP has been described most commonly in the area of the thoracotomy scar (Fig. 47.1) [17, 18]. It may also be noted in the ipsilateral pectoral region, subcostal areas, scapula and the ipsilateral arm and shoulder [17]. The pain of CPTP is usually described as a burning or numbness over the incision site [17–19]. Patients also describe a cutting, drawing or tender pain [20]. It may be constant or intermittent in nature although the more problematic forms of CPTP tend to be constant. The pain was noted to be exacerbated by such factors as lifting heavy objects. Interestingly, two authors also note that the pain is exacerbated by damp weather or rapid changes in weather [17, 18]. These weather-related changes are commonly reported in chronic pain clinics (authors note) and may be related to low pressure systems or frontal passage of weather systems with rapid shifts in barometric pressure.

Neuropathic pain is one of the most devastating forms of pain experienced by patients with chronic pain states (Fig. 47.2). Characterized by burning, lancinating, sharp or dysesthetic pain, it is the result of changes resulting in peripheral and central sensitization [21–23]. Steegers et al. [24] studied the type of pain experienced by those having CPTP and noted that 23% of patients with CPTP had definite neuropathic CPTP and a further 30% of patients with CPTP had some component of neuropathic pain. Approximately one half of persons suffering CPTP in this study had non-neuropathic pain. Those who had neuropathic pain tended to have more severe pain than those with persons with non-neuropathic pain [24].

A number of studies have examined the incidence of CPTP over the past 20 years [17, 18, 24–27]. The incidence of CPTP is consistently high. It has been reported as high as 81% at 3 months [17] to as low as 30–51% [20, 24, 25, 28]. The incidence varies considerably with type and intensity of pain reported.

While the overall incidence of CPTP is about one in two persons having thoracic surgery, there are some indications that the incidence of CPTP may be related to the efficacy of post-operative pain control [17, 26]. Katz et al. [26] reported that the risk of developing CPTP was related to the level of acute post-thoracotomy pain. Ochroch et al. [29] reported a 21% rate of CPTP after muscle-sparing thoracotomy (MT) with aggressive epidural analgesia. This low rate of CPTP was again reported by this group in a study of muscle-sparing vs. posterolateral thoracotomy with aggressive epidural analgesia [30]. While the overall incidence of CPTP is somewhat variable in the literature, the incidence of severe CPTP is consistent. Two to five percent of patients having thoracotomy will suffer severe CPTP 1 year after thoracotomy [17, 25, 26]. This is pain severe enough to interfere with a person's ability to carry out their daily activities.

The time course of CPTP has been reported in a number of studies [24, 25, 31–38]. Although the incidence of CPTP

FIG. 47.1. The most common locations of pain marked by patients after surgery.

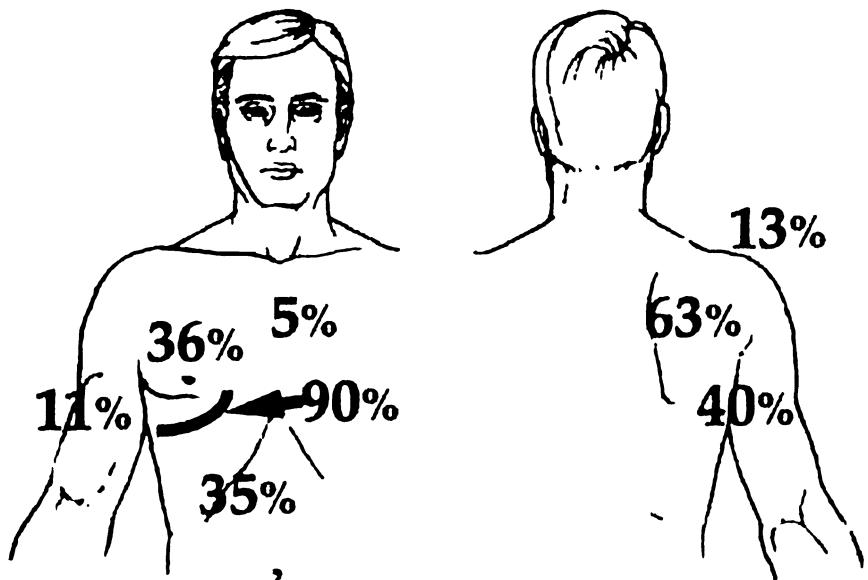
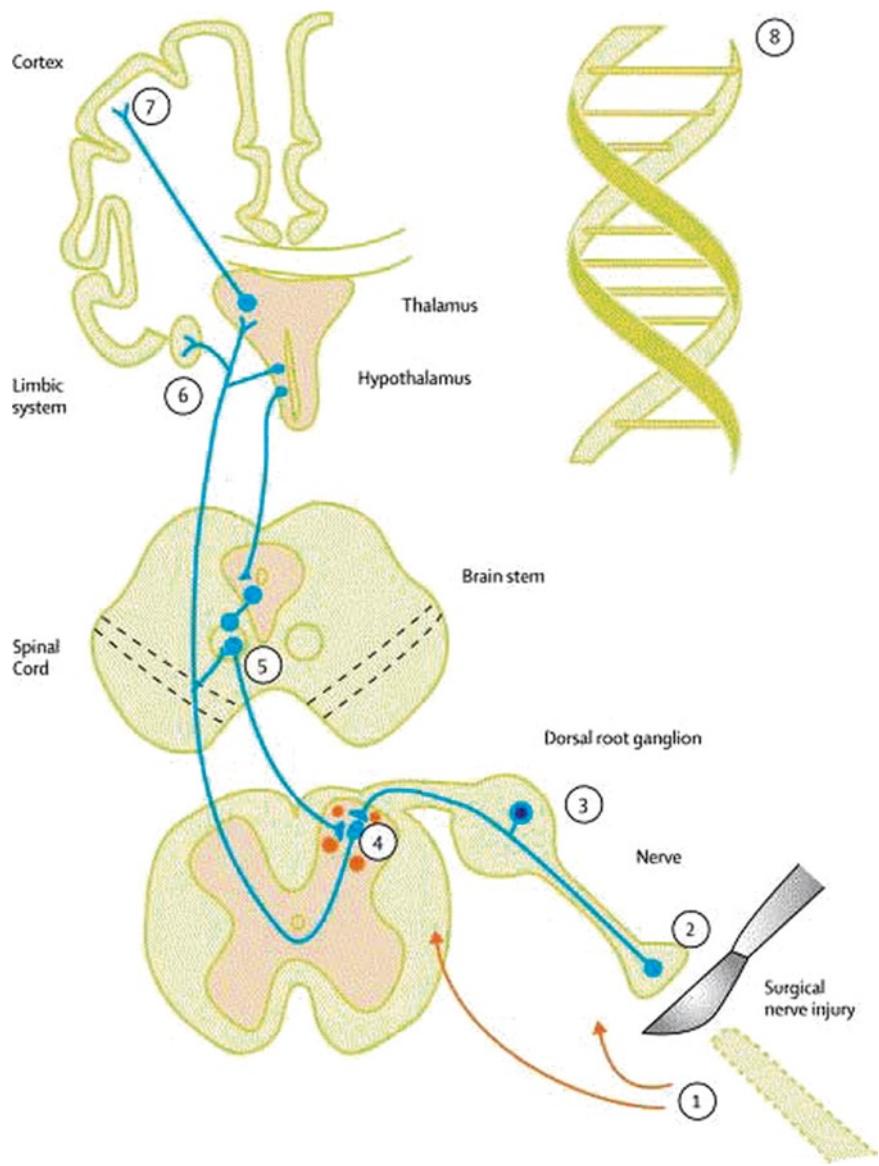


FIG. 47.2. Sites and mechanisms responsible for chronic postsurgical neuropathic pain.
 (1) Denervated Schwann cells and infiltrating macrophages distal to nerve injury produce local and systemic chemicals that drive pain signalling. (2) Neuroma at the site of injury is the source of ectopic spontaneous excitability in sensory fibres. (3) Changes in gene expression in dorsal root ganglion alter excitability, responsiveness, transmission, and survival of sensory neurons. (4) Dorsal horn is site of altered activity and gene expression, producing central sensitization, loss of inhibitory interneurons, and microglial activation, which together amplify sensory flow. (5) Brainstem descending controls modulate transmission in spinal cord. (6) Limbic system and hypothalamus contribute to altered mood, behaviour and autonomic reflexes. (7) Sensation of pain generated in cortex (past experiences, cultural inputs and expectations converge to determine what patient feels). (8) Genomic DNA predispose (or not) patient to chronic pain and affect their reaction to treatment (reprinted from Kehlet et al. [6], with permission from Elsevier.).



is initially high, the prevalence of CPTP appears to decrease over time [34, 36, 37]. In addition, the intensity of the pain seems to gradually decrease over time [29, 35]. Studies that track patients for a number of years indicate that the surviving patients tend to gradually improve with respect to the effect of pain on their lives [33, 37]. Although some patients may demonstrate declining pain over time, others may not show a decrease in their pain [37]. Thus, the average decline in reported pain level may be due to those who will eventually go on to have no pain, while others will have no relief from the CPTP. In a study of the neuropathic component of CPTP, Steegers et al. [24] demonstrated that the incidence of clear neuropathic pain declined after more than 3 years from surgery. However, while the incidence of overall CPTP demonstrates some decline over time, the incidence of severe CPTP, when reported, is stable [17, 26]. While not all studies of CPTP demonstrate this declining course of pain over time, the heterogeneity of patients, methods and disease states likely have a significant impact upon the reported prevalence of CPTP.

The Effect of Chronic Post-Thoracotomy Pain on Function

Chronic pain affects nearly every aspect of daily life. It interferes with the ability of the patient to sleep, work and interact with others. As such, it has a profound impact upon family life, emotional health and relationships with friends and co-workers. It is closely associated with depression and there is evidence that suicide risk is significantly increased in persons with chronic pain. Tang and Crane [39] demonstrated that persons with chronic pain have a risk of death by suicide twice that of controls and that the lifetime prevalence of suicide attempts was 5–14%. Those with chronic pain also have lower rates of self-rated health, an indicator of increased morbidity and mortality [40–42]. It may also be related to abnormal immune function [43, 44].

In addition to the impact that chronic pain has on individual sufferers, it has a significant impact on our society as a whole. Stewart et al. [45] estimated that common pain conditions in the USA were responsible for \$62.2 billion per year losses from lost productive time. Cost analysis of the impact in Canada in 1993 suggested that musculoskeletal pain conditions and injuries were responsible for economic losses of \$17.8 and \$14.3 billion annually. These costs would be significantly higher all these years later.

The impact of CPTP on individual function is, not surprisingly, significant. A number of studies have begun to address the impact of CPTP on function after thoracotomy [17, 29, 30, 35]. In a follow-up study of 111 thoracotomy patients, Pertunnen et al. [17] noted that half of patients were having difficulties with normal daily life 12 months after surgery. Only the severity of the limitation decreased with time. They also noted that sleep disturbances were present in 25–30% of patients with CPTP [17]. The impact of CPTP was assessed using the ten-question physical activity scale of the SF-36 [46, 47] at

intervals up to 49 weeks [29]. Activity levels at all intervals after surgery were significantly lower than the pre-operative levels. This is not surprising in the first few weeks after surgery, but as time progressed the level of activity reached a plateau and did not return to normal by 49 weeks. This was not related to the patient gender or the type of analgesic [29]. In a similar study comparing two types of incisions, the same group measured the impact of CPTP on function at 49 weeks using the Brief Pain Index (BPI) [48, 49] and the SF-36 [46, 47]. They determined that post-operative daily function was significantly lower than pre-operative function up to 49 weeks after surgery [30]. Maquire et al. [36] studied 610 patients who underwent thoracotomy an average of 26 months prior to the survey. Of these patients, nearly 40% were still taking analgesics, 45.5% believed that pain was their worst medical condition, 40% stated that pain limited their daily activities, 15% had attended a specialist pain clinic. The presence of a neuropathic component of the pain was associated with greater pain, increased analgesic use and more limitations of physical activity [36].

Those factors which play a role in the development of disability related to pain were studied by Katz et al. [50]. Utilizing a number of pain and disability measurement devices, they determined that pain intensity and emotional numbing predicted pain disability at 6 months after surgery. This changed over the subsequent 6 months as only the 12-month emotional numbing predicted pain disability at 12 months. Their results suggest a decoupling of pain intensity and pain disability. It also suggests that pain disability is more closely related to post-operative factors than to pre-operative factors or acute movement-related pain [27].

Clearly, the data suggest that CPTP has an impact upon the daily function of patients. It is clear that patients with neuropathic pain are affected more than those without neuropathic pain. The extent of the impact and its relationship to perioperative factors requires further characterization.

Factors Influencing the Development of Chronic Post-Thoracotomy Pain

Genetic Factors

The past 40 years has seen an explosion in the understanding of the genetics of illness, and attention has recently begun to turn to the enigma of pain. The human genome has been successfully mapped, and methods have been developed to map genes using computer modelling [51, 52]. In comparison, our understanding of the role of genetics in the sensation and experience of pain is vanishingly small. A short list of 23 genes was noted by LaCroix-Fralisch and Mogil [53] to be associated with experimental or clinical pain or analgesia.

Despite the lack of direct evidence, it is recognized that genetic variability may affect pain in a multitude of fashions. Pain susceptibility and the experience of pain may be

encoded differently. This has been demonstrated in low back pain [54], in a third molar extraction model and experimental pain states [53]. Indeed, the likelihood of developing a chronic pain state may be genetically mediated. Variants of the catecholamine-*O*-methyltransferase gene have been found to be linked to the risk of developing myogenous temporomandibular joint disorder [55]. There is also evidence that haplotype variation of GTP cyclohydrolase (GCH1), a rate-limiting enzyme for the production of tetrahydrobiopterin (BH4), is a marker for the variation in the regulation of pain sensitivity and chronicity mediated by BH4 [56]. Haplotype variation of GCH1, expressed as BH4, is associated with variation in pain after discectomy for persistent radicular pain [56]. Thus, early studies suggest that variability in human chronic pain conditions is modulated at the genetic level.

Genetic variability can affect the way that we respond to treatment in a number of ways. Both the pharmacodynamics and pharmacokinetics of pain treatment are governed by our genetic makeup. Examples of how the genetic modulation of pharmacokinetics may be found in the way that prodrugs are metabolized to active components, in the way that drugs are metabolized and in the way that they are transported across membranes [57]. Codeine and tramadol are both prodrugs that require activation [57]. Variation in the expression of CYPD6, responsible for the conversion of codeine to morphine and other metabolites, is responsible in large part for variability in the effectiveness of codeine [57, 58]. Tramadol metabolism is similarly responsible for the activity of the drug [59]. Pharmacodynamic variability may be expressed through variation in receptor expression or function. The mu receptor for morphine is perhaps the most studied and most relevant of the opioid receptors. It is also highly polymorphic and the polymorphism may manifest as requirements for higher or lower doses of opioids for pain management [57, 58, 60]. Other enzymes that may be involved in the metabolism of pain related medications include the cyclo-oxygenases and catechol-*O*-methyltransferase [57, 58].

Given that genetic study of pain is at a very early stage, it is therefore not surprising that specific data are lacking on the effects of genetic variability on CPTP. A multitude of questions remain to be addressed in the near future. These may include the effect of genetic variation on the response of patients to peri-operative pain management strategies, the response to chronic pain management strategies and ultimately upon the development of CPTP.

Surgical Factors

Posterolateral vs. Anterior Thoracotomy

Thoracic surgery can be performed in a number of ways. These include standard posterolateral thoracotomy (PLT), muscle-sparing thoracotomy (MT), antero-axillary thoracotomy (AAT), anterior limited thoracotomy (ALT) and

video-assisted thoracotomy (VATS) (Chaps. 22 and 23). Each method of accessing the thorax brings with it a unique set of challenges. The impact on the development of CPTP wrought by each method employed to access the thoracic cavity has been explored in a number of studies. The most common surgical method is open thoracotomy. Nomori et al. [31, 32] have examined the effect of the AAT and ALT on post-operative pain. In a study of 51 patients undergoing AAT or PLT for lung cancer, they reported pain in the immediate post-operative period and again at 1, 3 and 6 months [31]. They noted that patients having an AAT had significantly less pain on post-operative day (POD) 1, day 14, and at 1, 3 and 6 months after surgery than those persons undergoing PLT. Further, the percentage of patients with chronic pain after PLT was significantly higher than those receiving AAT [31]. This study was then extended by using the utilizing patients undergoing PLT or AAT as controls when examining a new procedure, the anterior limited thoracotomy (ALT), a variation on the AAT [32]. Unfortunately, the incidence of CPTP was not reported. ALT was noted to provide better early post-operative pain control than PLT and AAT. Post-operative pain at 1, 3 and 6 months was significantly better with either method of anterior thoracotomy than the standard PLT [32].

The axillary MT technique was compared to standard PLT in two studies [29, 30]. Data from the initial study [29] were re-examined and published again [30]. Patients were initially randomized to receive thoracic epidural analgesia (TEA) or placebo epidural. Surgical technique was chosen by the surgeon. The incidence of CPTP did not vary based on the type of incision, although other factors such as gender and acute pain were predictive of CPTP. Similarly, a study of 101 patients undergoing MT or PLT by Athanassiadi et al. [38] did not demonstrate a difference in the quantity of pain at 2 months. Unfortunately, the incidence of CPTP was not reported.

Video-Assisted Thoracoscopic Surgery (VATS)

For the past two decades, video-assisted thoracoscopic surgery (VATS) (Chap. 23) has been used with increasing frequency to perform a wide variety of surgical procedures. The procedure is minimally invasive and performed through multiple small ports rather than a single thoracotomy wound. Some procedures require the use of a “mini-thoracotomy”, to provide access. This may be associated with the use of a rib spreading device creating pressure on the neurovascular bundle. Furthermore the movement of the thoracoscope or surgical instruments within the port may create pressure on the neurovascular bundle.

The less invasive nature of the procedure is associated with less acute pain and more rapid recovery [61] and return to work [62]. However, the effect of VATS on chronic pain has been less clear. While few studies have directly compared the effects of VATS and thoracotomy on CPTP, it appears that the rates of chronic pain are relatively unchanged using this technique. In an early study of VATS and thoracotomy patients,

Landreneau et al. [63] surveyed patients for 3 or more months after their procedure. They noted that after 1 year there was no significant difference in the incidence of CPTP or rate of opioid treatment. However, patients who were less than 1 year from their procedure had significantly higher incidence of pain.

The rate and severity of CPTP following VATS may be related to the surgery conducted via the thoracoscope. Rates of CPTP vary widely from near zero to greater than 61% [24, 28, 33, 62, 64]. Two studies of thoracoscopic procedures for benign illness followed a group of patients for 10 years. The initial rate of CPTP was 20% after a mean follow-up of 34 months [64], declining to 12.5% after 10 years. Rates of CPTP after VATS surgery for lung cancer are generally reported to be much higher [28, 65]. This may be multifactorial in nature. Studies reporting pain are often reporting pain as a secondary outcome and patient populations are not standardized with respect to the type of surgery nor are the studies powered for pain outcomes. In addition, surgery for benign lung disease such as pneumothorax or bullectomy may require less surgical time and less vigorous manipulation of the instruments resulting in less compressive force on the neurovascular bundle. The length of surgery for lung cancer may also be longer for lung cancer surgery, resulting in more prolonged neurovascular bundle compression.

Thoracotomy in all of its forms involves traction or compression of the neurovascular bundle. Compression occurs as the rib spreader draws the ribs apart, as the VATS ports are torqued around the insertion site or as the paracostal sutures are tightened around the ribs in closure. Traction also occurs as the ribs are spread and the neurovascular bundle is stretched along the arc of the rib. The traction and compression of the bundle is thought to be the central injury resulting in post-thoracotomy neuropathic pain. The effect of injury on the neurovascular bundle and the intercostal muscle during thoracotomy, although yet to be fully elucidated, has been studied by a variety of methods. The superficial abdominal reflexes are, in part, mediated by the inferior intercostal nerves. Measurement of the abdominal reflexes after PLT indicates a strong correlation between the absence of reflexes and the intensity of post-operative pain including CPTP [66]. In a subsequent study, this group examined the effect of PLT and MT on neurophysiologic parameters [67]. They were able to demonstrate that the absence of abdominal reflexes and increased tactile threshold to electrical stimulation was tightly correlated to the intensity of CPTP [67]. Conversely, intra-operative studies of intercostal nerve motor evoked potentials have demonstrated nerve injury during thoracotomy, but have failed to derive a correlation to CPTP [68, 69].

Two further innovations in surgical technique continue to suggest a role for the neurovascular bundle and perhaps the intercostal muscle in the development of CPTP. Approximation of the ribs is commonly done using peri-costal sutures which wrap over the top of the superior rib and below the inferior rib, potentially resulting in a compression of the neurovascular bundle.

Closure using intracostal sutures, suturing through small holes drilled in the inferior rib, results in significantly less intense CPTP at 3 months [70]. Attempts to reduce the impact of retractor compression on the intercostal nerve by removing a muscle flap containing the neurovascular bundle from the inferior surface of the superior rib prior to retracting the ribs resulted in better post-operative spirometry and less pain at 3 months [71, 72]. This was further improved by leaving the muscle flap intact rather than cutting the distal end [72]. Hunt et al. [73] have also described a technique for protecting the neurovascular bundle from compression by the rib spreader as it is inserted into the wound. However, its effect on pain or other outcomes has yet to be studied. Thus, although controversy remains regarding the exact role of the intercostal nerve, neurovascular bundle and intercostal musculature in the development of CPTP, the current weight of evidence suggests that manoeuvres designed to reduce potential injury to these structures may reduce CPTP.

Factors Predicting CPTP

When investigating any chronic condition, the search for those factors which may be predictive of its development is the key. Identification of associated or predictive factors is important as it may allow identification of factors that are preventable or avoidable. In the case of CPTP a number of predictive factors have been investigated to determine whether there may be those factors that are preventable. The factor most commonly cited among post-operative chronic pain states is that of previous pain or acute post-operative pain. The presence of pain prior to surgery is associated with the development of chronic post-operative pain states [6, 16, 74]. This is clear in the case of hysterectomy [75, 76] and post-amputation pain [12, 13] as well as herniorrhaphy [6, 14, 74]. While pre-operative pain is associated with chronic pain in some states, it has not been clearly demonstrated to be predictive of development of CPTP [16, 24, 35–37]. However, the intensity of acute pain after thoracotomy is a significant predictor of CPTP [26, 37, 50]. Recently, Searle and colleagues [77] demonstrated that chronic neuropathic pain after thoracotomy is associated with acute neuropathic pain in the post-operative period. Emotional numbing has also been demonstrated as a predictor of pain disability at 6 and 12 months after lateral thoracotomy [27].

Age and gender have been implicated as predictors in a number of post-surgical pain conditions [5, 6]. Younger patients have a greater likelihood of developing post-surgical pain after herniorrhaphy [15, 78]. Similarly, age may be protective for persons undergoing thoracic surgery. In studies designed to seek out those factors which may predict the likelihood of developing CPTP, the effect of age has been consistent. Patients who develop CPTP tend to be younger than those who do not go on to develop chronic pain [24, 36, 37]. The risk of developing CPTP declines about 2% per year [36], although this may not be true across the entire age span as the vast majority of patients in studies are in their latter adult years.

While the effect of age on CPTP is clear, the effect of gender on CPTP is not yet certain. Some studies have indicated that women have a greater likelihood of developing CPTP after thoracic surgery [34, 35]. A study designed to determine the effect of gender on post-thoracotomy pain demonstrated that women were more likely to have pain 49 weeks after thoracotomy and that the pain would be of greater intensity [35]. It was also noted in the same study that older patients suffered less CPTP. However, worse pain in women has not been noted in all studies of CPTP. A number of studies including some designed specifically to determine factors predictive of CPTP have indicated that female gender is not a significant predictor for CPTP [20, 25, 36, 37]. Sample size may be a key factor in this disparity as the study demonstrating an effect of gender on CPTP [35] was the smallest of the studies to specifically seek out pre-operative predictors of CPTP.

One of the most exciting developments in recent years is the early stages of our understanding of the influence of pre-operative pain responses to painful stimuli, our pain threshold, as it were. Granot [79] reviewed studies of both static and dynamic responses to pain perception as predictors of post-operative pain, both acute and chronic. A number of studies of static pain parameters (tolerance, pain threshold, supra-threshold nociceptive stimuli) have been conducted in recent years and have demonstrated variable predictive capability [79–81] for acute post-operative pain as well as chronic post-operative pain [81]. This was specifically examined in the setting of CPTP [81].

The understanding of dynamic responses to pain, such as diffuse noxious inhibitory control (DNIC) an evaluation of the endogenous analgesia system, may lead to predictive testing capabilities. Yarnitsky et al. [81] evaluated DNIC in patients preparing to undergo thoracotomy. They demonstrated that those persons who have an efficient DNIC system are less likely to develop CPTP than persons with less efficient DNIC. Perhaps more importantly, this state is measurable pre-operatively [81]. This may provide a means to predict those with a propensity to CPTP and allow us to treat them accordingly.

The Influence of Analgesia Technique

Poor pain control after surgery has been identified as a factor in the development of long-term pain after surgery [26, 77]. This is true for thoracic surgery as well as other surgical procedures. A number of methods of pain management may be employed to manage post-thoracotomy pain in the peri-operative period. These include local anesthetic rib blocks, intrathecal local anesthetics or opioids, intravenous patient-controlled analgesia, thoracic epidural analgesia (TEA) and paravertebral blocks. The most common of these is paravertebral catheter. A catheter is placed in the paravertebral space either percutaneously by the anaesthetist or intra-operatively by the surgeon. Local anaesthetics are then administered by bolus or infusion, providing a unilateral block covering a

number of spinal levels. The paravertebral catheter has been compared to TEA in a number of studies of post-thoracotomy pain and found to be equivalent [82–87]. No studies to date have been published on the effects of paravertebral blockade on CPTP.

Thoracic epidural analgesia is a standard method for pain management after thoracotomy in many institutions. A catheter is inserted in the thoracic epidural space somewhere between the T5/T6 interspace and the T7/T8 interspace. The catheter is placed via a Tuohy needle and placement is confirmed by testing the development of an appropriate block with a small amount of lidocaine (20–40 mg). The position of the tip of the catheter can be determined using an electrical current, the Tsui test [88]. In the peri-operative period local anaesthetics, usually bupivacaine or ropivacaine, opioids such as morphine or hydromorphone alone or in combination are used to maintain a continuous epidural blockade over the area including the thoracotomy site.

The effect of peri-operative epidural analgesia on CPTP has been the subject of a small number of studies [29, 89–91]. These studies have examined initiation of epidural analgesia before and after thoracotomy incision [29, 89, 91, 92]. These studies evaluated the effects of different local anaesthetic combinations and opioid medications. These studies have included prospective follow-up studies as well as randomized controlled trials of different methods of administering TEA [89, 91]. However, not all studies of TEA demonstrated improvement in CPTP [29]. A meta-analysis of the effects of pre-emptive TEA on post-thoracotomy pain did not find sufficient evidence to state that pre-emptive TEA reduced CPTP [93]. Furthermore, recent studies have demonstrated that anaesthesia including TEA with the addition of low-dose intravenous ketamine is effective at reducing peri-operative pain, but it is not effective in the prevention of CPTP [94, 95]. However, a number of factors may influence this finding. Some of the studies did not state a clear sample size calculation so they may be underpowered for the results obtained. Further, there is evidence that only about one half of CPTP is neuropathic in nature [24]. It may be that the portion of CPTP most affected by early analgesia is the neuropathic pain. If that is true, then all of the studies of TEA and CPTP so far will be underpowered. Clearly, there is an opportunity for further study here.

Prevention and Treatment of CPTP

Management of CPTP, like any pain condition, should begin with prevention. Linear logic would suggest that review of predictive factors should provide a clear path to prevention. However, the reality seems to be more complex. While many factors are associated with the development of CPTP, it is not yet possible to determine clear causality of any single factor. Acute pain is clearly associated with CPTP but to date, strategies to reduce acute pain such as TEA and paravertebral blockade have had mixed success in the prevention of CPTP [93].

Changes in surgical practice may provide some advantage in the prevention of CPTP but this remains to be demonstrated in large clinical trials [70, 72]. Despite the lack of evidence for prevention of CPTP good clinical practice dictates that we take all reasonable measures to ameliorate acute pain and prevent, if possible, CPTP. To that end many institutions; including the authors have embarked on a multimodal peri-operative regimen. Such regimens consist of comprehensive pain management strategies in the intra-operative period, usually TEA or PVB, as well as medical therapy usually started before surgery. Although gabapentin is yet to be proven as efficacious in preventing CPTP, it has been demonstrated to be effective in the treatment of CPTP [96]. Thus, some regimens for pre-operative medical management of peri-operative pain consist of gabapentin in combination with other analgesics such as acetaminophen, tricyclic antidepressants and/or slow release forms of oral opioids. Intra-operatively, TEA or paravertbral blockade is utilized. In the case of TEA, while evidence is not conclusive [91, 93], it is reasonable to initiate the blockade prior to incision. This is not possible in the case of surgeon placed paravertebral blockade as these typically placed under direct vision through the thoracotomy wound. Continued attention to pain management throughout the peri-operative period with the addition of appropriate medications including opioids as necessary is paramount. Regular follow-up in the months following surgery with attention to pain management is also prudent.

Treatment of CPTP, like any other chronic condition, begins with assessment of the type and cause of the pain. As with any form of chronic pain, it is important to search for reversible causes of CPTP. Foremost among these in persons having CPTP is the search for recurrence of tumour. This is true at the first and each subsequent patient visit after thoracotomy. Tumour recurrence may be heralded by a change or progression in the pain, or by new onset pain. However, even in those persons who seem otherwise unchanged, it remains wise to continue to consider recurrence of tumour or development of new neoplasm as potential cause of the pain. Treatment for the pain of tumour is different from that of chronic non-cancer pain after thoracotomy and may include chemotherapy or radiation therapy.

Patients presenting post-operatively to surgical clinics or to their primary care practitioner should be evaluated for post-operative pain at each visit. In the early post-operative period patients should receive appropriate analgesic therapy for their pain. This may include anti-epileptic medications, tricyclic antidepressants and opioids. Those patients with persistent pain lasting more than 3 months after surgery should be considered as candidates for referral to a multidisciplinary pain clinic. Again, this should take place after tumour recurrence has been ruled out.

Having established that the pain is not from tumour or other reversible condition (e.g., lung herniation [97] or occult rib fracture), it is important to determine whether the pain is of neuropathic origin. A number of screening tools exist to assist in the diagnosis of neuropathic pain [98]. Use of these tools

on a regular basis may assist in the development of a comprehensive treatment plan.

A number of guidelines have been published regarding the treatment of neuropathic pain disorders [99–101]. The guidelines delineate pharmacologic treatment into first-, second- and third-line medications [99, 101, 102]. First-line pharmacotherapy typically includes antidepressant medications beginning with tricyclic anti-depressants (TCA), serotonin-norepinephrine reuptake inhibitors (SNRI), gabapentinoids and topical lidocaine. Second-line treatments include opioid analgesics and tramadol formulations [99, 101]. Recent studies have demonstrated significant benefit to prescribing combination pharmacotherapy for the treatment of neuropathic pain [103]. Combination therapy of gabapentin with the SNRI duloxetine and a cholinesterase inhibitor, donepezil, has demonstrated a synergistic interaction on an experimental neuropathic pain in rats [104]. Further studies on such combinations are necessary to determine the clinical efficacy of these combinations.

Recent studies of CPTP treatment have demonstrated that gabapentin is effective in the treatment of post-thoracotomy pain [96, 105]. Interestingly, Solak et al. [96] specifically studied patients with neuropathic pain after thoracotomy and demonstrated the effectiveness of gabapentin. Other treatments that have been reported include etodolac alone or in combination with topical nitroglycerin [106]. This study demonstrated effectiveness of the treatment combination for neuropathic CPTP but has not been repeated. The addition of further medications such as a TCA or SNRI in this setting may have an additive treatment effect although this has not been studied in CPTP.

Other therapies for management of CPTP include such modalities as transcutaneous electrical nerve stimulation (TENS). A recent review of this modality has supported its use in management of CPTP [107]. Acupuncture has been evaluated in the peri-operative setting and found to be ineffective in reducing post-thoracotomy pain [108]. However, it has not been tested in the setting of CPTP.

In summary, while no established method of prevention of CPTP has been described, careful attention to peri-operative pain management including a multimodal analgesia regimen is prudent. Careful follow-up, again with attention to pain management and exclusion of reversible causes of pain, including tumour is the second phase of prevention and management of CPTP. In those persons who go on to have pain for more than 3 months of duration, it is recommended that the patients receive the attentions of a multidisciplinary pain clinic.

Clinical Case Discussion

Mrs. D., a 59-year-old woman, was referred to the Pain Management Clinic by her surgeon with a complaint of right-sided chest pain in the area of her thoracotomy scar. Six months before she underwent a VATS right upper lobe lobectomy for Stage I non-small cell lung carcinoma.

Past Medical/Surgical History

The patient had a history of 30 pack years of smoking, having quit 2 years prior to surgery. She had hypertension and diabetes mellitus type II managed by diet therapy. Her pre-operative medications consisted of hydrochlorothiazide 12.5 mg and daily ASA 82 mg.

Peri-Operative Course

Her intra-operative course was uneventful and mediastinal lymph node biopsies were negative. One hour prior to surgery she received gabapentin 600 mg and acetaminophen 1000 mg. Mrs. D. received intra-operative intercostal blocks and patient-controlled analgesia for peri-operative pain management. Her chest tube was removed on day 3, and she was discharged home on day 7. Nursing notes recorded an average pain score in the first 24 h of 8/10. Pain scores gradually decreased to 5/10 at discharge.

Visit 1

At the time of presentation, she described a burning, stabbing pain in the area of the thoracotomy scar. Recent chest radiograph and CT scan were negative for recurrent malignancy. She rated the pain as an average of 5/10. She stated that “good days” brought a pain level of 4/10, and “bad days” brought pain at a level of 7–8/10. She had considerably more bad days than good. The pain radiated to the scapula and anterior chest wall. Her sleep was interrupted by the pain and she was unable to return to her work as a cashier. Treatment at the time of presentation consisted of two acetaminophen 325 mg/oxycodone 5 mg combination tablets four times daily.

Examination revealed allodynia in the area of the scar. The wound appeared to have healed otherwise well. No other abnormalities were noted.

A diagnosis of post-thoracotomy chronic pain was made and a multidisciplinary treatment plan was discussed. The treatment plan was as follows:

1. The patient was referred for rehabilitation physiotherapy and acupuncture. TENS therapy was explained, and written instructions were provided along with a prescription for a TENS unit and pads.
2. She was started on nortriptyline 25 mg qhs. Recommendations were made to her primary care provider to start gabapentin at 300 mg qhs, increasing to 600–1800 mg t.i.d.
3. She was referred to the local pain self-management program, consisting of physiotherapy, occupational therapy, psychology, diet therapy and vocational therapy.
4. A follow-up appointment was made for 6 months.

Visit 2

Mrs. D. reports that she had moderate relief with the nortriptyline at 2 weeks and a further improvement with the addition of gabapentin gradually increased to a dose of 600 mg three

times daily. Further dose increases were limited by dizziness. Her average pain was now rated at a 3/10 with occasional pain-free days and maximum pain at 5–6/10. Attendance at the pain self-management programme provided useful strategies for managing pain and allowed her to return to work part-time. TENS therapy was intermittently useful for breakthrough pain.

After repeat chest X-ray and CT confirmed no evidence of recurrence a prescription for topical lidocaine was provided. A follow-up appointment was set for 6 months.

Visit 3

Mrs. D. visited the clinic 6 months after her initial visit. She was regularly using the nortriptyline and gabapentin. Intermittent use of topical lidocaine had improved control of her neuropathic pain on “bad days”. Her family physician had added hydromorphone long-acting formulation at 3 mg twice daily. She felt that this was helpful with minimal side effects. A recent visit to the surgeon and oncologist showed no evidence of recurrence. She had recently returned to her volunteer work at her church.

References

1. Crambie IK, Davies HT, Macrae WA. Cut and thrust: antecedent surgery and trauma among patients attending a chronic pain clinic. *Pain*. 1998;76(1–2):167.
2. Macrae WA. Chronic pain after surgery. *Br J Anaesth*. 2001; 87(1):88.
3. Macrae WA. Chronic post-surgical pain: 10 years on. *Br J Anaesth*. 2008;101(1):77.
4. Burke S, Shorten G. When pain after surgery doesn't go away *Biochem Soc Trans*. 2009;37(1):318.
5. Eisenberg E. Post-surgical neuralgia. *Pain*. 2004;111(1–2):3.
6. Kehlet H, Jensen T, Woolf C. Persistent postsurgical pain: risk factors and prevention. *Lancet*. 2006;367(9522):1618.
7. Vilhjalmsson OJ, Cold S, Rasmussen L, Sindrup SH. Sensory function and pain in a population of patients treated for breast cancer. *Acta Anaesthesiol Scand*. 2009;53(6):800.
8. Poleshuck E, Katz J, Andrus C, Hogan L, Jung B, Kulick D, et al. Risk factors for chronic pain following breast cancer surgery: a prospective study. *J Pain*. 2006;7(9):626.
9. Steegers MA, Wolters B, Evers AW, Strobbe L, Wilder-Smith OH. Effect of axillary lymph node dissection on prevalence and intensity of chronic and phantom pain after breast cancer surgery. *J Pain*. 2008;9(9):813.
10. Amichetti M, Caffo O. Pain after quadrantectomy and radiotherapy for early-stage breast cancer: incidence, characteristics and influence on quality of life. Results from a retrospective study. *Oncology*. 2003;65(1):23.
11. Flor H. Phantom-limb pain: characteristics, causes, and treatment. *Lancet Neurol*. 2002;1(3):182.
12. Nikolajsen L, Jensen TS. Phantom limb pain. *Br J Anaesth*. 2001;87(1):107.
13. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain*. 1985;21(3):267.

14. Aasvang EK, Bay-Nielsen M, Kehlet H. Pain and functional impairment 6 years after inguinal herniorrhaphy. *Hernia*. 2006;10(4):316.
15. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth*. 2005;95(1):69.
16. Wildgaard K, Ravn J, Kehlet H. Chronic post-thoracotomy pain: A critical review of pathogenic mechanisms and strategies for prevention. *Eur J Cardiothorac Surg*. 2009;36:170–80.
17. Perttunen K, Tasimuth T, Kalso E. Chronic pain after thoracic surgery: a follow-up study. *Acta Anaesthesiol Scand*. 1999; 43(5):563.
18. Dajczman E, Gordon A, Kreisman H, Wolkove N. Long-term postthoracotomy pain. *Chest*. 1991;99(2):270.
19. Hazelrigg S, Cetindag I, Fullerton J. Acute and chronic pain syndromes after thoracic surgery. *Surg Clin North Am*. 2002;82(4):849.
20. Kalso E, Perttunen K, Kaasinen S. Pain after thoracic surgery. *Acta Anaesthesiol Scand*. 1992;36(1):96.
21. Baron R. Neuropathic pain: a clinical perspective. *Handb Exp Pharmacol*. 2009;194:3.
22. O'Connor A. Neuropathic pain: quality-of-life impact, costs and cost effectiveness of therapy. *Pharmacoeconomics*. 2009; 27(2):95.
23. Costigan M, Scholz J, Woolf C. Neuropathic pain: a maladaptive response of the nervous system to damage. *Annu Rev Neurosci*. 2009;32:1.
24. Steegers MAH, Snik DM, Verhagen AF, van der Drift MA, Wilder-Smith OHG. Only half of the chronic pain after thoracic surgery shows a neuropathic component. *J Pain*. 2008; 9(10):955.
25. Pluijms WA, Steegers MAH, Verhagen AFTM, Scheffer GJ, Wilder-Smith OHG. Chronic post-thoracotomy pain: a retrospective study. *Acta Anaesthesiol Scand*. 2006;50(7):804.
26. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain*. 1996;12(1):50.
27. Katz J, Asmundson GJG, McRae K, Halket E. Emotional numbing and pain intensity predict the development of pain disability up to one year after lateral thoracotomy. *Eur J Pain*. 2009;13(8):870.
28. Furrer M, Rechsteiner R, Eigenmann V, Signer C, Althaus U, Ris HB. Thoracotomy and thoracoscopy: postoperative pulmonary function, pain and chest wall complaints. *Eur J Cardiothorac Surg*. 1997;12(1):82.
29. Ochroch EA, Gottschalk A, Augostides J, Carson K, Kent L, Malayaman N, et al. Long-term pain and activity during recovery from major thoracotomy using thoracic epidural analgesia. *Anesthesiology*. 2002;97(5):1234.
30. Ochroch EA, Gottschalk A, Augostides J, Aukburg S, Kaiser L, Shrager J. Pain and physical function are similar following axillary, muscle-sparing vs posterolateral thoracotomy. *Chest*. 2005;128(4):2664.
31. Nomori H, Horio H, Fuyuno G, Kobayashi R. Non-serratus-sparing antero-axillary thoracotomy with disconnection of anterior rib cartilage. improvement in postoperative pulmonary function and pain in comparison to posterolateral thoracotomy. *Chest*. 1997;111(3):572.
32. Nomori H, Horio H, Suemasu K. Anterior limited thoracotomy with intrathoracic illumination for lung cancer: its advantages over anteroaxillary and posterolateral thoracotomy. *Chest*. 1999;115(3):874.
33. Stammberger U, Steinacher C, Hillinger S, Schmid RA, Kinsberger T, Weder W. Early and long-term complaints following video-assisted thoracoscopic surgery: evaluation in 173 patients. *Eur J Cardiothorac Surg*. 2000;18(1):7.
34. Gotoda Y, Kambara N, Sakai T, Kishi Y, Kodama K, Koyama T. The morbidity, time course and predictive factors for persistent post-thoracotomy pain. *Eur J Pain*. 2001;5(1):89.
35. Ochroch EA, Gottschalk A, Troxel AB, Farrar JT. Women suffer more short and long-term pain than men after major thoracotomy. *Clin J Pain*. 2006;22(5):491.
36. Maguire MF, Ravenscroft A, Beggs D, Duffy JP. A questionnaire study investigating the prevalence of the neuropathic component of chronic pain after thoracic surgery. *Eur J Cardiothorac Surg*. 2006;29(5):800.
37. Gottschalk A, Ochroch EA. Clinical and demographic characteristics of patients with chronic pain after major thoracotomy. *Clin J Pain*. 2008;24(8):708.
38. Athanassiadi K, Kakaris S, Theakos N, Skottis I. Muscle-sparing versus posterolateral thoracotomy: a prospective study. *Eur J Cardiothorac Surg*. 2007;31(3):496.
39. Tang NKY, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychol Med*. 2006;36(5):575.
40. Mossey JM, Shapiro E. Self-rated health: a predictor of mortality among the elderly. *Am J Public Health*. 1982;72(8):800.
41. Kaplan GA, Goldberg DE, Everson SA, Cohen RD, Salonen R, Tuomilehto J, et al. Perceived health status and morbidity and mortality: evidence from the kuopio ischaemic heart disease risk factor study. *Int J Epidemiol*. 1996;25(2):259.
42. Idler EL, Benyamin Y. Self-rated health and mortality: a review of twenty-seven community studies. *J Health Soc Behav*. 1997;38(1):21.
43. Liebeskind JC. Pain can kill. *Pain*. 1991;44(1):3.
44. Watkins LR, Maier SF. Immune regulation of central nervous system functions: from sickness responses to pathological pain. *J Intern Med*. 2005;257(2):139.
45. Stewart W, Ricci J, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290:2443.
46. Ware JE, Sherbourne CD. 36-Item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473.
47. Ware JE. SF-36 health survey update. *Spine*. 2000;25(24):3130.
48. Cleeland CS, Ryan KM. Pain assessment: global use of the brief pain inventory. *Ann Acad Med Singapore*. 1994;23(2):129.
49. Tittle M, McMillan S, Hagan S. Validating the brief pain inventory for use with surgical patients with cancer. *Oncol Nurs Forum*. 2003;30(2):325.
50. Katz J, Asmundson GJ, McRae K, Halket E. Emotional numbing and pain intensity predict the development of pain disability up to one year after lateral thoracotomy. *Eur J Pain*. 2008;13:870–8.
51. Yu B. In silico gene discovery. *Methods Mol Med*. 2008;141:1.
52. Yu B. Role of in silico tools in gene discovery. *Mol Biotechnol*. 2009;41(3):296.
53. Lacroix-Fralish M, Mogil J. Progress in genetic studies of pain and analgesia. *Annu Rev Pharmacol Toxicol*. 2009;49:97.
54. Tegeder I, Ltsch J. Current evidence for a modulation of low back pain by human genetic variants. *J Cell Mol Med*. 2009;13:1605–19.
55. Diatchenko L, Slade G, Nackley A, Bhalang K, Sigurdsson A, Belfer I, et al. Genetic basis for individual variations in pain

- perception and the development of a chronic pain condition. *Hum Mol Genet.* 2005;14(1):135.
56. Tegeder I, Costigan M, Griffin R, Abele A, Belfer I, Schmidt H, et al. GTP cyclohydrolase and tetrahydrobiopterin regulate pain sensitivity and persistence. *Nat Med.* 2006;12(11):1269.
57. Ltsch J, Geisslinger G, Tegeder I. Genetic modulation of the pharmacological treatment of pain. *Pharmacol Ther.* 2009; 124(2):168.
58. Diatchenko L, Nackley A, Tchivileva I, Shabalina S, Maixner W. Genetic architecture of human pain perception. *Trends Genet.* 2007;23(12):605.
59. Garrido M, Sayar O, Segura C, Rapado J, Dios-Vieitez M, Renedo M, et al. Pharmacokinetic/pharmacodynamic modeling of the antinociceptive effects of (+)-tramadol in the rat: role of cytochrome P450 2D activity. *J Pharmacol Exp Ther.* 2003;305(2):710.
60. Ltsch J, Geisslinger G. Relevance of frequent mu-opioid receptor polymorphisms for opioid activity in healthy volunteers. *Pharmacogenomics J.* 2006;6(3):200.
61. Grogan EL, Jones DR. VATS lobectomy is better than open thoracotomy: what is the evidence for short-term outcomes? *Thorac Surg Clin.* 2008;18(3):249.
62. Bertrand PC, Regnard JF, Spaggiari L, Levi JF, Magdeleinat P, Guibert L, et al. Immediate and long-term results after surgical treatment of primary spontaneous pneumothorax by VATS. *Ann Thorac Surg.* 1996;61(6):1641.
63. Landreneau RJ, Mack MJ, Hazelrigg SR, Naunheim K, Dowling RD, Ritter P, et al. Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg.* 1994;107(4):1079.
64. Hutter J, Miller K, Moritz E. Chronic sequels after thoracoscopic procedures for benign diseases. *Eur J Cardiothorac Surg.* 2000;17(6):687.
65. Handy JR, Asaph JW, Douville EC, Ott GY, Grunkemeier GL, Wu Y. Does video-assisted thoracoscopic lobectomy for lung cancer provide improved functional outcomes compared with open lobectomy? *Eur J Cardiothorac Surg.* 2010;37:451–5.
66. Benedetti F, Amanzio M, Casadio C, Filosso PL, Molinatti M, Oliari A, et al. Postoperative pain and superficial abdominal reflexes after posterolateral thoracotomy. *Ann Thorac Surg.* 1997;64(1):207.
67. Benedetti F, Vighetti S, Ricco C, Amanzio M, Bergamasco L, Casadio C, et al. Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. *J Thorac Cardiovasc Surg.* 1998;115(4):841.
68. Rogers ML, Henderson L, Mahajan RP, Duffy JP. Preliminary findings in the neurophysiological assessment of intercostal nerve injury during thoracotomy. *Eur J Cardiothorac Surg.* 2002;21(2):298.
69. Maguire MF, Latter JA, Mahajan R, Beggs FD, Duffy JP. A study exploring the role of intercostal nerve damage in chronic pain after thoracic surgery. *Eur J Cardiothorac Surg.* 2006;29(6):873.
70. Cerfolio RJ, Price TN, Bryant AS, Sale Bass C, Bartolucci AA. Intracostal sutures decrease the pain of thoracotomy. *Ann Thorac Surg.* 2003;76(2):407.
71. Cerfolio RJ, Bryant AS, Patel B, Bartolucci AA. Intercostal muscle flap reduces the pain of thoracotomy: a prospective randomized trial. *J Thorac Cardiovasc Surg.* 2005;130(4):987.
72. Cerfolio RJ, Bryant AS, Maniscalco LM. A nondivided intercostal muscle flap further reduces pain of thoracotomy: a prospective randomized trial. *Ann Thorac Surg.* 2008;85(6):1901.
73. Hunt I, Thakar C, Anikin V. Reducing post-thoracotomy wound pain by limited mobilisation of the intercostal muscle neurovascular bundle prior to wound retraction. *Ann R Coll Surg Engl.* 2008;90(7):616.
74. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology.* 2000; 93(4):1123.
75. Brandsborg B, Nikolajsen L, Hansen C, Kehlet H, Jensen T. Risk factors for chronic pain after hysterectomy: a nationwide questionnaire and database study. *Anesthesiology.* 2007;106(5):1003.
76. Brandsborg B, Dueholm M, Nikolajsen L, Kehlet H, Jensen T. A prospective study of risk factors for pain persisting 4 months after hysterectomy. *Clin J Pain.* 2009;25(4):263.
77. Searle RD, Simpson MP, Simpson KH, Milton R, Bennett MI. Can chronic neuropathic pain following thoracic surgery be predicted during the post-operative period? *Interact Cardiovasc Thorac Surg.* 2009;9:999–1002.
78. Poobalan A, Bruce J, Smith WCS, King P, Krukowski Z, Chambers WA. A review of chronic pain after inguinal herniorrhaphy. *Clin J Pain.* 2003;19(1):48.
79. Granot M. Can we predict persistent postoperative pain by testing preoperative experimental pain? *Curr Opin Anaesthesiol.* 2009;22(3):425.
80. Weissman-Fogel I, Granovsky Y, Crispel Y, Ben-Nun A, Best L, Yarnitsky D, et al. Enhanced presurgical pain temporal summation response predicts post-thoracotomy pain intensity during the acute postoperative phase. *J Pain.* 2009;10(6):628.
81. Yarnitsky D, Crispel Y, Eisenberg E, Granovsky Y, Ben-Nun A, Sprecher E, et al. Prediction of chronic post-operative pain: pre-operative DNIC testing identifies patients at risk. *Pain.* 2008;138(1):22.
82. Scarci M, Joshi A, Attia R. In patients undergoing thoracic surgery is paravertebral block as effective as epidural analgesia for pain management? *Interact Cardiovasc Thorac Surg.* 2010;10(1):92.
83. Daly DJ, Myles PS. Update on the role of paravertebral blocks for thoracic surgery: are they worth it? *Curr Opin Anaesthesiol.* 2009;22(1):38.
84. Garutti I, González-Aragoneses F, Biencinto MT, Novoa E, Simón C, Moreno N, et al. Thoracic paravertebral block after thoracotomy: comparison of three different approaches. *Eur J Cardiothorac Surg.* 2009;35:829–32.
85. Gulbahar G, Kocer B, Muratlı S, Yıldırım E, Gulbahar O, Dural K, et al. A comparison of epidural and paravertebral catheterisation techniques in post-thoracotomy pain management. *Eur J Cardiothorac Surg.* 2010;37:467–72.
86. Conlon NP, Shaw AD, Grichnik KP. Postthoracotomy paravertebral analgesia: will it replace epidural analgesia? *Anesthesiol Clin.* 2008;26(2):369.
87. Richardson J, Cheema S. Thoracic paravertebral nerve block. *Br J Anaesth.* 2006;96(4):537.
88. Tsui BC, Gupta S, Finucane B. Confirmation of epidural catheter placement using nerve stimulation. *Can J Anesth.* 1998;45(7):640.
89. Senturk M, Ozcan P, Talu G, Kiyan E, Camci E, Ozyalin S, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg.* 2002;94(1):11.
90. Tiippuna E, Nilsson E, Kalso E. Post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. *Acta Anaesthesiol Scand.* 2003;47(4):433.

91. Obata H, Saito S, Fujita N, Fuse Y, Ishizaki K, Goto F. Epidural block with mepivacaine before surgery reduces long-term post-thoracotomy pain. *Can J Anesth.* 1999;46(12):1127.
92. Ochroch EA, Gottschalk A. Impact of acute pain and its management for thoracic surgical patients. *Thorac Surg Clin.* 2005;15(1):105.
93. Bong C, Samuel M, Ng J, Ip-Yam C. Effects of preemptive epidural analgesia on post-thoracotomy pain. *J Cardiothorac Vasc Anesth.* 2005;19(6):786.
94. Suzuki M. Low-dose intravenous ketamine potentiates epidural analgesia after thoracotomy. *Anesthesiology.* 2006;105(1):111.
95. Dualé C, Sibaud F, Guastella V, Vallet L, Gimbert YA, Taheri H, et al. Perioperative ketamine does not prevent chronic pain after thoracotomy. *Eur J Pain.* 2009;13:197–505.
96. Solak O, Metin M, Esme H, Solak O, Yaman M, Pekcolaklar A, et al. Effectiveness of gabapentin in the treatment of chronic post-thoracotomy pain. *Eur J Cardiothorac Surg.* 2007;32(1):9.
97. DiMarco AF, Oca O, Renston JP. Lung herniation. A cause of chronic chest pain following thoracotomy. *Chest.* 1995;107(3):877.
98. Bennett M, Attal N, Backonja M, Baron R, Bouhassira D, Freynhagen R, et al. Using screening tools to identify neuropathic pain. *Pain.* 2007;127(3):199.
99. O'Connor A, Dworkin R. Treatment of neuropathic pain: an overview of recent guidelines. *Am J Med.* 2009;122(10 Suppl):S22.
100. Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. *Cochrane Database Syst Rev* 2007;(4):CD005454.
101. Attal N, Cruccu G, Haanp M, Hansson P, Jensen TS, Nurmikko T, et al. EFNS guidelines on pharmacological treatment of neuropathic pain. *Eur J Neurol.* 2006;13(11):1153.
102. Dworkin R, O'Connor A, Backonja M, Farrar J, Finnerup N, Jensen T, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain.* 2007;132(3):237.
103. Gilron I, Bailey J, Tu D, Holden R, Jackson A, Houlden R. Nor-triptyline and gabapentin, alone and in combination for neuropathic pain: a double-blind, randomised controlled crossover trial. *Lancet.* 2009;374(9697):1252.
104. Hayashida K, Eisenach J. Multiplicative interactions to enhance gabapentin to treat neuropathic pain. *Eur J Pharmacol.* 2008;598(1–3):21.
105. Sihoe ADL, Lee T, Wan IYP, Thung K, Yim APC. The use of gabapentin for post-operative and post-traumatic pain in thoracic surgery patients. *Eur J Cardiothorac Surg.* 2006;29(5):795.
106. Glantz L. Efficacy of transdermal nitroglycerin combined with etodolac for the treatment of chronic post-thoracotomy pain: an open-label prospective clinical trial. *J Pain Symptom Manage.* 2004;27(3):277.
107. Freynet A, Falcoz P. Is transcutaneous electrical nerve stimulation effective in relieving postoperative pain after thoracotomy? *Interact Cardiovasc Thorac Surg.* 2010;10(2):283.
108. Deng G, Rusch V, Vickers A, Malhotra V, Ginex P, Downey R, et al. Randomized controlled trial of a special acupuncture technique for pain after thoracotomy. *J Thorac Cardiovasc Surg.* 2008;136(6):1464.

Principles and Practice of Anesthesia for Thoracic Surgery

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To Lee, Luke and Rusty. Thanks, P.

Preface

This book, *The Principles and Practice of Anesthesia for Thoracic Surgery*, is designed to be a comprehensive and up-to-date reference text for all aspects of anesthesia related to noncardiac intrathoracic diagnostic and therapeutic procedures. The goal of this text is to improve the perioperative care of thoracic surgical patients. It is written for practitioners of thoracic anesthesia at all levels: Residents, Fellows, Staff Anesthesiologists, Nurse Anesthetists, Nurse Practitioners, Anesthesia Assistants, and Allied Health Professionals who are involved in managing these patients.

The spectrum of patients who require anesthesia for thoracic procedures continues to evolve. At the beginning of the last century, thoracic surgery was mainly performed for infectious diseases and their complications such as empyema, bronchiectasis, and broncho-pleural fistula. This continues to be the mainstay of thoracic anesthesia in many developing countries as described by Dr. Rebecca Jacob of Bengaluru, India, in Chap. 33. Occasionally, patients with these types of pathology present for surgery in hospitals in the developed world also, so the principles of lung separation and isolation for these cases remain fundamental building blocks of thoracic anesthesia.

By the middle of the last century, the spectrum of thoracic surgery had shifted so that the majority of patients are now patients with malignancies, particularly lung cancer. As the population changes so have the surgical procedures; from pneumonectomy and lobectomy to lung-sparing procedures such as segmentectomy. And the surgical techniques have evolved from open thoracotomies to minimally invasive video-assisted thoracic surgery (VATS). This has allowed thoracic surgeons and chest physicians to expand the envelope of patients considered operable and to offer potentially curative pulmonary resections to patients with increasingly severe comorbidities. This in turn has placed a greater emphasis on the need for anesthesiologists to manage one-lung ventilation in complicated patients. VATS, and now Robotic, procedures have expanded to include esophageal, vertebral, cardiac, and other types of intrathoracic surgery. Practitioners who work in centers that do not perform lung surgery may now be required to provide anesthesia for VATS procedures.

The beginning of this century heralds the evolution of procedures for end-stage lung disease. Lung transplantation, lung volume reduction, whole-lung lavage, and pulmonary thromboendarterectomy are all examples of this new spectrum of operations for patients who require safe perioperative anesthetic care. Attendant with this expansion of surgery are new techniques and tools that the anesthesiologist must be familiar with such as transesophageal echocardiography, interventional lung assist devices, ex vivo lung perfusion, alternatives for postoperative analgesia, and lung isolation in patients with difficult airways. All of these are described in this text.

All of the clinical chapters in this text have been organized with a Clinical Case Discussion at the end. The purpose of these cases is to review the material presented in the preceding chapter and then to allow the reader to compare his/her solution to the clinical problem with that of the chapter authors. This should allow the reader to reflect on what has been discussed in the text and to get an impression of how the presented material can be applied in a clinical context.

This text begins, at the beginning, with the History of Thoracic Anesthesia in Chap. 1. This excellent and insightful introduction is written by Ian Conacher of Newcastle, England who has recently retired but has been a leading authority on thoracic anesthesia in Britain for the past several decades.

Next is a section on Preoperative Evaluation which details the basics of preoperative assessment focused on patients presenting for thoracic surgery, specifically pulmonary resection.

I am grateful to Gail Darling, Professor of Thoracic Surgery at the University of Toronto, for her help with this chapter. And also a chapter on Thoracic Imaging by Javier Campos and Kalpaj Parekh of the University of Iowa. Javier is a world expert on lung isolation and his use of 3-D CT scans to predict difficult placement of double-lumen tubes and bronchial blockers highlights how important it is for the clinician practicing thoracic anesthesia to examine and understand the patient's chest imaging prior to surgery. This is one of four excellent chapters he has contributed to this text.

The next major section deals with issues of anatomy, physiology, pharmacology, and perioperative lung injury common to essentially all thoracic patients. Respiratory physiology is vitally important, fascinating, and puzzling to most anesthesiologists and in no context does this apply more than during one-lung anesthesia. Drs. Jaeger, Blank, Lohser, and Ishikawa have synthesized the recent advances in our understanding of this complex area and present it in a fashion that allows for clinical application. This is one of several chapters with contributions from Randy Blank who has been a part of this project from the very first concept and has also helped immensely by recruiting several of his colleagues from the outstanding Anesthesiology Department at the University of Virginia to contribute chapters. Similarly, this book has major excellent contributions from Jens Lohser and the very progressive Thoracic Anesthesia group at the Vancouver General Hospital. Recent research on the active contributions of the pulmonary system to metabolism and pharmacologic modifications of respiratory airway and vascular responses are detailed in Chaps. 7–9 by Drs. Littlewood, Wojciechowski, Hurford, Reimer, and Granton. Dr. Granton is head of the Pulmonary Hypertension program at the University of Toronto and a world authority in the area. Chapter 10 deals with perioperative lung injury which is becoming the major cause of mortality after major pulmonary resections.

The next section, Chaps. 11–13, of the text is devoted to anesthetic management of surgical procedures on the airways. Foreign bodies, the use of lasers in the airway and tracheal resections are anxiety provoking for all involved. Endo-bronchial ultrasound is a recent diagnostic technique that may replace mediastinoscopy for some patients. These chapters offer an organized approach to managing these difficult problems. I am indebted to Ron Purugganan (Chap. 12) for his contribution on current intravenous anesthetic techniques for managing these airway cases. This is one of two chapters (also Chap. 19 on Monitoring by Gabriel Mena) from the very busy Thoracic Anesthesia group at the MD Anderson Cancer Center in Houston.

The next section, Chaps. 14 and 15, covers Mediastinal procedures including mediastinoscopy, resection of mediastinal masses, thymic disorders (specifically myasthenia gravis), and parathyroid disorders related to lung malignancies. Mediastinal masses and myasthenia are always stressful for the anesthesiologist and I am grateful to Min Ku (Singapore) and Liza Chelico (Toronto) for their organized approaches to these difficult topics.

The next section, Chaps. 16–23, deals with Anesthetic Management of common intrathoracic procedures. Lung Isolation (Chap. 16) and the specific problem of Lung Isolation in Patients with Difficult Airways (Chap. 17) are thoroughly presented with excellent illustrations. Chapter 18 presents a detailed approach to preventing neurologic injuries during thoracic surgery. Chapters 19 and 20 deal with advances in monitoring. Chapter 20 specifically deals with the increased applications of transesophageal echocardiography during thoracic surgery. I am very grateful to my colleagues in the Anesthesia Department of the University of Toronto and the Toronto General Hospital: Max Meineri (Chap. 20), Karen McRae (Chap. 13), Martin Ma (Chap. 24), and Marcin Wasowicz (Chap. 32) without whose contributions and support this text would not have been possible. Chapter 21 by Denham Ward provides a detailed review of intraoperative ventilation management in the context of Thoracic Surgery. Chapter 22 by Drs. Ochroch et al. presents a unique and useful systems approach to management of major pulmonary resections. Chapter 23 by Edmond Cohen, the Director of Thoracic Anesthesia at Mt. Sinai Hospital NY, discusses anesthetic management for the ever-increasing spectrum of VATS procedures.

The next section, Chaps. 24–26, deals with anesthesia for thoracic procedures in patients with significant comorbidities or in the elderly. Increasingly, the thoracic surgical population has patients with advanced age or morbid obesity. Drs. Castillo, Port and Heerd (Chap. 25), and Brodsky (Chap. 26) are acknowledged experts in these areas.

Chapters 27–32 deal with uncommon and complex thoracic surgical procedures such as extrapleural pneumonectomy, combined pulmonary/vertebral resections, esophageal resections, robotic surgery, and combined cardiac and pulmonary surgery. In Chap. 28, Ju-Mei Ng summarizes the large clinical experience of the Brigham and Women's Hospital, Boston, with extrapleural pneumonectomy. Chapter 29 by Drs. Kaufman, Amar, and Rusch is one of two excellent chapters (also Chap. 44 by Drs. Amar and Pedoto) by the very active Thoracic Anesthesia and Surgery Departments from the Memorial Sloan-Kettering Cancer Center in New York.

Chapters 33–35 cover thoracic surgical and therapeutic procedures which are less common but still form a basic part of thoracic anesthesia such as broncho-pleural fistula, bullectomy, hydatid cysts, massive hemoptysis, and broncho-pulmonary lavage. I am particularly thankful to Jean Bussières, University of Laval, Quebec, for sharing his large experience in whole-lung lavage.

The next section Chaps. 36–38 deals with anesthetic management of thoracic surgery for end-stage lung diseases: Lung Volume Reduction (Erin Sullivan, Pittsburgh), Lung Transplantation (Andy Roscoe, Manchester, UK), and Pulmonary Thrombo-endarterectomy (Gerry Manecke, San Diego). These chapters encompass the leading edge of anesthetic management for these severely ill patients.

Chapter 39 is directed to the specific issues and pathologies related to thoracic surgery in pediatrics. This comprehensive chapter by Drs. Schwartz and Karsli from the Hospital for Sick Children, here in Toronto, covers lung isolation in pediatrics, tracheo-esophageal fistula, diaphragmatic hernia, and the entire range of problems in children and infants that may require thoracic surgery either in a large teaching hospital or in a smaller regional center. Chapter 40 by Stephen Panaro provides a useful systematic approach to anesthesia for the patient with Thoracic Trauma.

The final section, Chaps. 41–47, deals with topics in the area of thoracic postoperative care that the anesthesiologist may be required to manage. These include immediate complications such as cardiac herniation (Chap. 41) and Respiratory Failure (Chap. 42). Chapter 43 by Vera von Dossow-Hanfstingl and a group of Anesthesiologists from Munich and Berlin gives an exciting look at the increasing use of modern technology, beyond standard ventilatory support, such as interventional lung assist to manage respiratory failure in these patients. Chapter 44 gives a detailed look at cardiac complications after thoracic surgery. Chapter 45 on postthoracotomy surgical management includes what every anesthesiologist needs to know in this area, particularly about chest drainage systems. I thank Dirk Wagnetz and Marc de Perrot of our own Thoracic Surgical Division for this chapter. Chapter 46 by Drs. Pennefather and McKeivith, Liverpool, UK, is a thorough presentation of multimodal analgesia after thoracic surgery and the wide-range of available options. The final chapter by Peter MacDougall, Dalhousie University, Halifax, deals with the increasingly recognized problem of chronic post-thoracotomy pain.

I hope that the reader of this text whether involved in a University or Community practice will be able to increase their comprehension of the issues related to thoracic anesthesia and this in turn will benefit their patients.

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Toronto, May 2011

Peter Slinger

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Part X

Anesthesia for Pediatric Thoracic
Surgical Procedures

Part XI

Trauma

Part XII

Post-Operative Management