

function, pain, disability, and fear avoidance behavior.^{54,55} On the other hand, passive treatments like massage or chiropractic interventions are not beneficial.⁵⁶ The regimen of graded exercise follows the original concept of Fordyce.¹⁹ Patients are instructed to find a baseline tolerance level for each exercise. Next, a program of improvement is negotiated and agreed upon. Patients note improvements on a daily basis and are required to complete the exercise plan regardless of how they feel. Thus, the control over exercise behavior is contingent upon plan rather than pain, since exercise and pain are disconnected. Individual motivation is an important factor determining how well patients learn to manage pain.⁵⁷

Occupational Therapy

The occupational therapist teaches the patient to achieve life goals despite pain and to overcome the limitations imposed by pain. Occupational therapy assessment includes a history of working life and place, family life, and daily activities, as well as a physical examination to determine range-of-motion and the presence of movement disorders or deformities that might hinder performance. The primary therapeutic objectives are reduction of pain and associated disability, promotion of optimal function in everyday life, and the encouragement of meaningful family, social, and work relationships.⁵⁸ An important target is supporting the patient's return to work including specific work conditioning.⁵⁹ The chance of returning to work after a period of sick leave from low back pain, for example, apparently decreases over time, thereby generating enormous cost to society through wage compensation, social support, and loss of production.³¹ Barriers to return to work include job dissatisfaction and perceptions of the impact of work on the cause of pain. Together with the patient, the occupational therapist should develop a program to increase self-esteem, restore self-efficacy, and promote optimal occupational and recreational function despite pain.

Anesthesiology

The role of the anesthesiologist in the treatment of chronic pain has changed considerably over the last decades. "Nerve block practices" have been replaced by interdisciplinary pain management centers. In this context the anesthesiologist acts as both a physician-educator and a technical expert. The challenge is to optimally complement regional anesthesia skills and pharmacologic knowledge with the psychosocial components of chronic pain to render more comprehensive pain management services. Anesthesiologists need to use their expertise in pharmacotherapy, nerve blocks, and skilled techniques within the broad-based biopsychosocial approach. The focus is not only on reducing pain but also on decreasing disability, improving quality of life, and increasing function. The conventional way of administering medication "as needed" or to use nerve blocks for short-term pain relief may risk reinforcement of pain behavior, and the patient's belief in an underlying physical abnormality that is best managed by biomedical procedures.⁴² Moreover, false expectations are maintained; for example, the patient cannot be the passive recipient, but must be an active participant in the process. Patients may believe that pain is the primary problem in the patient's life. This neglects psychosocial factors, perpetuates the expensive and futile search for unidimensional

biomedical solutions, and promotes iatrogenic somatization, medicalization, and high health care use by chronic pain patients.⁴² The role of the anesthesiologist within the interdisciplinary team differs depending on the type of patient being treated. Cancer and acute pain management demand the full range of the anesthesiologist's technical skills and pharmacologic knowledge. In chronic nonmalignant pain, the anesthesiologist's abilities as an educator, coach, and motivator are far more important. As a member of the interdisciplinary team, the anesthesiologist has to reinforce and maintain the biopsychosocial focus, respond appropriately to somatic concerns, and manage medications. In concert with the other members of the team, the anesthesiologist uses motivational strategies to encourage the patient to attain self-managed reactivation goals in physical, psychosocial, recreational, and vocational domains. At the same time, the anesthesiologist's presence provides "white coat credibility" and is essential to avoid the patient's pejorative conclusion that the pain is "all in my head." The anesthesiologist monitors the patient's physical status, potential development of new medical problems, and medications. In addition, the anesthesiologist provides real-time reassurance and education regarding the absence of relevant abnormality, the minimal role of surgery, and conveys medical information to make informed choices. The anesthesiologist plays a crucial role within the multidisciplinary team to direct the patient toward a multimodal pain treatment plan and to coordinate this program. The majority of pain therapists worldwide are anesthesiologists. They work closely with other healthcare professionals in this setting, thereby gaining added recognition outside the operating room.⁴²

Drugs Used for Chronic Pain

Analgesic drugs interfere with the generation or transmission (or both) of impulses following noxious stimulation in the nervous system (nociception). This can occur at both the peripheral and central levels of the neuraxis. The therapeutic aim is to diminish the perception of pain. Analgesics aim at modulating either the formation of noxious chemicals (e.g., prostaglandins) or the activation of neuronal receptors or ion channels transducing or transmitting noxious stimuli (e.g., peptide, kinin, monoamine receptors, Na^+ channels). Drugs currently used in chronic pain include opioids, nonsteroidal antiinflammatory drugs (NSAIDs), serotonergic compounds, antiepileptics, and antidepressants (Table 51.1). Local anesthetics are used for local and regional anesthetic techniques. Mixed drugs combine different mechanisms, for example noradrenaline reuptake inhibition and opioid agonist effects (tramadol, tapentadol), or opioid agonist and NMDA antagonist effects (ketamine). Various routes of drug administration (e.g., oral, intravenous, subcutaneous, intrathecal, epidural, topical, intraarticular, transmucosal) can be used, depending on the clinical circumstances. In addition, placebo treatments have shown significant analgesic effects, mediated by opioid and nonopioid mechanisms.⁶⁰ Chronic pain requires a multidisciplinary approach encompassing both pharmacologic and nonpharmacologic (psychological, physiotherapeutic) treatment strategies (see "Interdisciplinary Management of Chronic Pain").

TABLE 51.1 Analgesic Drugs, Targets, Mechanisms, and Side Effects

Drugs	Targets	Mechanisms	Functional Consequences	Side Effects
Opioids	G-protein coupled μ -, δ -, κ -receptors	↓ cAMP ↓ Ca^{++} currents ↑ K^{+} currents	↓ Excitability of peripheral and central neurons ↓ Release of excitatory neurotransmitters	μ , δ : sedation, nausea, euphoria/reward, respiratory depression, constipation κ : dysphoria/aversion, diuresis, sedation
NSAIDs	cyclooxygenases (COX-1, COX-2)	↓ prostaglandins ↓ thromboxanes	↓ Sensitization of sensory neurons ↑ Inhibition of spinal neurons	Nonselective: gastrointestinal ulcers, perforation, bleeding, renal impairment COX-2: thrombosis, myocardial infarction, stroke
Serotonin agonists	G-protein coupled 5-HT receptors 5-HT ₃ ; ion channels	↓ cAMP (5-HT ₁) ↑ cAMP (5-HT ₄₋₇) ↑ PLC (5-HT ₂)	↓ Release of excitatory neuropeptides ↓ Neurogenic inflammation ↑ Vasoconstriction	Myocardial infarction, stroke, peripheral vascular occlusion
Antiepileptics	Na^{+} , Ca^{++} channels GABA receptors	↓ Na^{+} currents ↓ Ca^{++} currents ↑ GABA receptor activity	↓ Excitability of peripheral and central neurons ↓ Release of excitatory neurotransmitters	Sedation, dizziness, cognitive impairment, ataxia, hepatotoxicity, thrombocytopenia
Antidepressants	Noradrenaline/5-HT transporters Na^{+} , K^{+} channels	↓ Noradrenaline/5-HT reuptake ↓ Na^{+} currents ↑ K^{+} currents	↓ Excitability of peripheral and central neurons	Cardiac arrhythmia, myocardial infarction, sedation, nausea, dry mouth, constipation, dizziness, sleep disturbance, blurred vision

NSAIDs, Nonsteroidal antiinflammatory drugs; GABA, γ -aminobutyric acid (GABA).

OPIOIDS

Opioids act on heptahelical G-protein-coupled receptors. Three types of opioid receptors (μ , δ , κ) have been cloned. Several subtypes (e.g., μ_1 , μ_2 , δ_1 , δ_2), possibly resulting from gene polymorphisms, splice variants, or alternative processing have been proposed. Opioid receptors are localized and can be activated along all levels of the neuraxis including peripheral and central processes of primary sensory neurons (nociceptors), spinal cord (interneurons, projection neurons), brainstem, midbrain, and cortex. All opioid receptors couple to G-proteins (mainly G_i/G_o) and subsequently inhibit adenylyl cyclase, decrease the conductance of voltage-gated Ca^{++} channels, or open rectifying K^{+} channels, or any combination of these actions (Fig. 51.3a).⁶¹ These effects ultimately result in decreased neuronal activity. The prevention of Ca^{++} influx inhibits the release of excitatory (pronociceptive) neurotransmitters. A prominent example is the suppression of substance P release from primary sensory neurons, both within the spinal cord and from their peripheral terminals within injured tissue. At the postsynaptic membrane, opioids produce hyperpolarization by opening K^{+} channels, thereby preventing excitation or propagation of action potentials in second-order projection neurons. In addition, opioids inhibit sensory neuron-specific tetrodotoxin-resistant Na^{+} channels, TRPV1 channels, and excitatory postsynaptic currents evoked by glutamate receptors (e.g., NMDA) in the spinal cord. The result is decreased transmission of nociceptive stimuli at all levels of the neuraxis and profoundly reduced perception of pain. Endogenous opioid receptor ligands are derived from the precursors proopiomelanocortin (encoding β -endorphin), proenkephalin (encoding Met-enkephalin and Leu-enkephalin), and prodynorphin (encoding dynorphins). These peptides contain the common Tyr-Gly-Gly-Phe-Met/Leu sequence at their amino terminals, known as the opioid motif. β -Endorphin and the enkephalins are

potent antinociceptive agents acting at μ - and δ -receptors. Dynorphins can elicit both pro- and antinociceptive effects via NMDA receptors and κ -opioid receptors, respectively. A fourth group of tetrapeptides (endomorphins) with yet unknown precursors do not contain the pan-opioid motif but bind to μ -receptors with high selectivity. Opioid peptides and receptors are expressed throughout the central and peripheral nervous system, in neuroendocrine tissues, and in immune cells.^{9,62} Extracellular opioid peptides are susceptible to rapid enzymatic inactivation by aminopeptidase N and neutral endopeptidase. Both peptidases are expressed in the central nervous system, peripheral nerves, and leukocytes and, among opioids, enkephalins are considered their preferred substrates. Preventing the extracellular degradation of endogenous opioid peptides by peptidase inhibitors, both in central and peripheral compartments, has been shown to produce potent analgesic effects in many animal models and in some small human trials.^{63,64}

The commonly available opioid drugs (morphine, codeine, methadone, fentanyl and its derivatives) are μ -agonists. Naloxone is a nonselective antagonist at all three receptors. Partial agonists must occupy a greater fraction of the available pool of functional receptors than full agonists to induce a response of equivalent magnitude. Mixed agonist/antagonists (buprenorphine, butorphanol, nalbuphine, pentazocine) may act as agonists at low doses and as antagonists (at the same or a different receptor type) at higher doses. Such compounds typically exhibit ceiling effects for analgesia and they may elicit an acute withdrawal syndrome when administered together with a pure agonist. All three receptors (μ , δ , κ) mediate analgesia but differing side effects. μ -Receptors mediate respiratory depression, sedation, reward/euphoria, nausea, urinary retention, biliary spasm, and constipation. κ -Receptors mediate dysphoric, aversive, sedative, and diuretic effects. δ -Receptors mediate reward/euphoria, respiratory depression, convulsions,

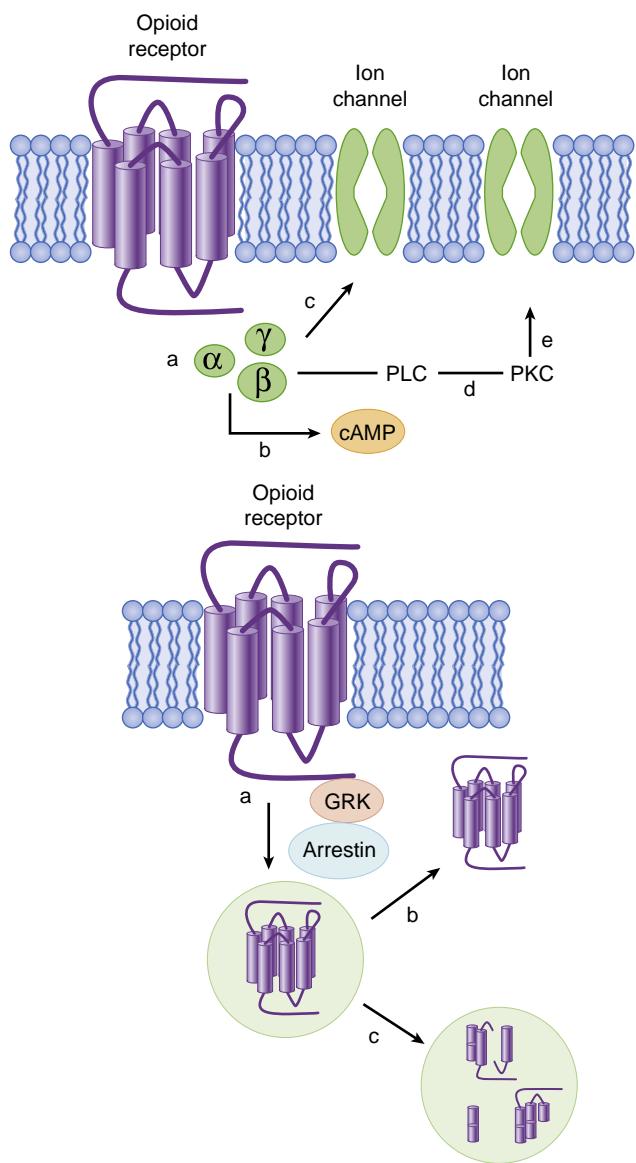


Fig. 51.3 Opioid receptor signaling and recycling. Upper panel: Opioid ligands induce a conformational change at the receptor which allows coupling of G proteins to the receptor. The heterotrimeric G-protein dissociates into active G_{α} and $G_{\beta\gamma}$ subunits (a) which can inhibit adenylyl cyclase and reduce cAMP (b), decrease the conductance of voltage-gated Ca^{++} channels, or open rectifying K^{+} channels (c). In addition, the phospholipase C/phosphokinase C pathways can be activated (d) to modulate Ca^{++} channel activity in the plasma membrane (e). Lower panel: Opioid receptor desensitization and trafficking is activated by G protein-coupled receptor kinases (GRK). After arrestin binding, the receptor is in a desensitized state at the plasma membrane (a). Arrestin-bound receptors can then be internalized via a clathrin-dependent pathway, and either be recycled to the cell surface (b) or degraded in lysosomes (c). (Adapted from Zöllner C, Stein C. Opioids. *Handb Exp Pharmacol*. 2007;(177):31–63. ²⁰⁴)

and constipation.^{65–67} Immunosuppressive effects of opioids were frequently proposed in experimental studies but have not been verified in clinical outcome trials.^{68,69}

Tolerance describes the phenomenon that the magnitude of a given drug effect decreases with repeated administration of the same dose, or that increasing doses are needed to produce the same effect. Tolerance is not synonymous with dependence. Physical dependence is defined as a state

of adaptation that is manifested by a withdrawal syndrome elicited by abrupt cessation, rapid dose reduction, and/or administration of an antagonist.⁷⁰ All opioids produce clinically relevant physical dependence, even when administered only for a relatively short period of time.⁷¹ All opioid effects (e.g., analgesia, nausea, respiratory depression, sedation, constipation) can be subject to tolerance development, albeit to different degrees. For example, tolerance to respiratory depression, sedation, and nausea often develops faster than to constipation or miosis.^{66,67,72,73} Incomplete cross-tolerance between opioids or genetic differences may explain clinical observations that switching drugs (“opioid rotation”) is occasionally useful in patients with inadequate pain relief or intolerable side effects.⁷⁴ Opioid-induced adaptations occur at multiple levels in the nervous and other organ systems, beginning with direct modulation of opioid receptor signaling and extending to complex neuronal networks including learned behavior. Proposed mechanisms involved in pharmacodynamic tolerance include opioid receptor-G-protein uncoupling, decreased receptor internalization/recycling, and increased sensitivity of the NMDA receptor (see Fig. 51.3b).⁶¹ In addition, pharmacokinetic (e.g., altered distribution or metabolism of the opioid) and learned tolerance (e.g., compensatory skills developed during mild intoxication) as well as increased nociceptive stimulation by tumor growth, inflammation, or neuroma formation are possible reasons for increased dose requirements.^{72,75} There is a lack of carefully controlled studies that unequivocally demonstrate pharmacodynamic tolerance to opioid analgesia (i.e., reduction of clinical pain) in patients.^{76,77}

There is an ongoing debate whether opioids may paradoxically induce hyperalgesia. However, many studies have, in fact, shown withdrawal-induced hyperalgesia, a well-known phenomenon following the abrupt cessation of opioids.^{78–80} At high doses, occasionally encountered in extreme cancer pain, singular cases of allodynia have been observed and attributed to neuroexcitatory effects of opioid metabolites.⁸¹ There is no conclusive evidence that hyperalgesia occurs during the perioperative or chronic administration of regular opioid doses in patients.^{77,78,82,83}

Opioids are effective in the periphery (e.g., topical or intraarticular administration, particularly in inflamed tissue), at the neuraxis (intrathecal, epidural, or intracerebroventricular administration), and systemically (intravenous, oral, subcutaneous, sublingual, or transdermal administration).¹⁸ The clinical choice of a particular compound or its formulation is based on pharmacokinetic considerations (route of administration, desired onset or duration, lipophilicity) and on side effects associated with the respective route of drug delivery.¹⁸ Dosages are dependent on patient characteristics, type of pain, and route of administration. Systemically and spinally administered opioids can produce similar side effects, depending on dosage and rostral/systemic redistribution. For intrathecal application lipophilic drugs are preferred because they are trapped in the spinal cord and less likely to migrate to the brain within the cerebrospinal fluid. Adverse side effects can be minimized by careful dose titration and close patient monitoring, or can be treated by co-medication (antiemetics, laxatives) or opioid receptor antagonists (e.g., naloxone). No significant side effects have been reported for the peripheral (e.g., topical) application of small, systemically inactive doses of opioids.

Opioids are considered the most effective analgesics for severe acute (e.g., postoperative) and cancer-related chronic pain. However, the long-term use of opioids in chronic noncancer (e.g., neuropathic, musculoskeletal, abdominal) pain is highly controversial. Randomized controlled trials (RCTs) have only been conducted for a maximum period of 3 months. In meta-analyses, the reduction of pain scores was clinically insignificant and epidemiological data suggest that quality of life or functional capacity are not improved.⁸⁴⁻⁸⁶ A recent meta-analysis of RCTs of patients with chronic noncancer pain, evidence from high-quality studies showed that opioid use was associated with statistically significant but small improvements in pain and physical functioning, and increased risk of vomiting compared with placebo.^{86a} In this meta-analysis comparisons of opioids with nonopioid alternatives suggested that the benefit for pain and functioning may be similar, although the evidence was from studies of only low to moderate quality. Adverse side effects (nausea, sedation, constipation, dizziness, etc.) and lack of analgesic efficacy led to the dropout of high numbers of subjects, both in RCTs and in uncontrolled observational studies beyond 3 months.⁸⁶ Psychosocial outcome variables were rarely investigated and showed only modest improvement. Thus, consistent with the multifactorial nature of chronic pain, opioids alone probably cannot produce an analgesic response. Clearly, the entire patient must be evaluated, not just the pain.⁸⁷ The target of intervention is not only the source of nociception (if at all identifiable) but suffering, dysfunction, psychosocial factors, and dependence on the healthcare system. In addition, addiction has been reported in high numbers of patients treated with opioids for chronic pain, and overdoses, death rates, and abuse of prescription opioids have become a public health problem.^{84,88} Thus, the use of opioids as a sole treatment modality in chronic nonmalignant pain is strongly discouraged.⁴⁷

NONSTEROIDAL ANTIINFLAMMATORY DRUGS AND ANTIPYRETIC ANALGESICS

NSAIDs and antipyretic analgesics (e.g., acetaminophen, phenazones) inhibit COX, the enzymes that catalyze the transformation of arachidonic acid (a ubiquitous cell component generated from phospholipids) to prostaglandins and thromboxanes.⁸⁹ Two isoforms, COX-1 and COX-2, are constitutively expressed in peripheral tissues and in the central nervous system. In response to injury and inflammatory mediators (e.g., cytokines, growth factors) both isoforms can be upregulated, resulting in increased concentrations of prostanoids. In the periphery, prostanoids (mainly PGE₂) sensitize nociceptors by phosphorylation of ion channels (e.g., Na⁺, TRPV1) via EP receptor activation. As a result, nociceptors become more responsive to noxious mechanical (e.g., pressure, hollow organ distension), chemical (e.g., acidosis, bradykinin, neurotrophic factors), or thermal stimuli. In the spinal cord PGE₂ blocks glycinergic neuronal inhibition, enhances excitatory amino acid release, and depolarizes ascending neurons. These mechanisms facilitate the generation of impulses within nociceptors and their transmission through the spinal cord to higher brain areas. By blocking COX, prostanoid formation

diminishes. Subsequently, nociceptors become less responsive to noxious stimuli and spinal neurotransmission is attenuated.

Less severe pain states (e.g., early arthritis, headache) are commonly treated with nonselective NSAIDs (e.g., aspirin, ibuprofen, indomethacin, diclofenac) or antipyretic analgesics (e.g., acetaminophen), mostly used orally. Some drugs are available for parenteral, rectal, or topical application. Over-the-counter availability and self-medication have led to frequent abuse and toxicity.⁸⁹ Adverse side effects are attributed to COX-1-induced blockade of thromboxane production and impairment of platelet function (gastrointestinal and other bleeding disorders), decrease of tissue-protective prostanoids (gastrointestinal ulcers, perforation), decrease of renal vasodilatory prostanoids (nephrotoxicity), and to formation of highly reactive metabolites (acetaminophen hepatotoxicity). The development of selective COX-2 inhibitors was driven by the assumption that COX-2 expression is selectively induced in inflamed tissue and that the constitutive tissue-protective COX-1 would be spared. It has now become clear that COX-2 expression is constitutive in many tissues (e.g., gastrointestinal epithelium, vascular endothelium, spinal cord) and COX-2 inhibition may exacerbate inflammation, impair ulcer healing, and decrease formation of vasoprotective prostacyclin. COX inhibitors confer an increased risk of thrombosis, myocardial infarction, renal impairment, hypertension, stroke, and liver toxicity, and can cause rare anaphylactic reactions.

NSAIDs and antipyretic analgesics play a controversial role in chronic pain. For example, their uncontrolled use may result in medication overuse headache.⁹⁰ In chronic degenerative musculoskeletal pain, their use is disputed⁹¹ and they are not indicated in neuropathic pain.⁹²

SEROTONERGIC DRUGS

Serotonin (5-hydroxytryptamine; 5-HT) is a monoamine neurotransmitter found in the sympathetic nervous system, in the gastrointestinal tract, and in platelets. It acts on 5-HT receptors expressed at all levels of the neuraxis and on blood vessels. Within the dorsal horn of the spinal cord serotonergic neurons contribute to endogenous pain inhibition. With the exception of 5-HT₃ (a ligand-gated ion channel), 5-HT receptors are G-protein coupled receptors. 5-HT_{1B/1D} agonists (triptans) have been studied extensively and are effective against neurovascular (migraine, cluster) headaches. Migraine is thought to be related to the release of neuropeptides (e.g., calcitonin gene-related peptide) from trigeminal sensory neurons innervating meningeal and intracranial blood vessels. This leads to vasodilation, an inflammatory reaction, and subsequent pain. Triptans inhibit neurogenic inflammation via 5-HT_{1D} receptors on trigeminal afferents, with possible additional sites of action on thalamic neurons and in the periaqueductal grey. The activation of vascular 5-HT_{1B} receptors constricts meningeal (and coronary) vessels. The latter effects have stimulated a search for alternative approaches such as targeting calcitonin-gene-related-peptide or highly selective 5HT_{1F} agonists.⁹³ Triptans can be applied orally, subcutaneously, or transnasally and have been used in the treatment of migraine. All triptans narrow coronary arteries via 5-HT_{1B} receptors at clinical doses and should not be administered

to patients with risk factors or coronary, cerebrovascular, or peripheral vascular disease. Many compounds have the potential for significant drug-drug interactions.⁹³

ANTIEPILEPTIC DRUGS

Antiepileptics are used in neuropathic pain resulting from lesions to the peripheral (e.g., diabetes, herpes) or central (e.g., stroke) nervous system and for migraine prophylaxis. Neuropathic syndromes have been attributed to ectopic activity in sensitized nociceptors from regenerating nerve sprouts, recruitment of previously “silent” nociceptors, or spontaneous neuronal activity (or any combination of these processes). These events may result in sensitization of primary afferents and subsequent sensitization of second- and third-order ascending neurons. Among the best studied mechanisms are the increased expression and trafficking of ion channels (e.g., Na^+ , Ca^{++} , TRP) and increased activity at glutamate (NMDA) receptor sites. The mechanisms of action of antiepileptics include neuronal membrane stabilization by blockage of pathologically active voltage-sensitive Na^+ channels (e.g., carbamazepine, lamotrigine, topiramate), blockage of voltage-dependent Ca^{++} channels (gabapentin, pregabalin), inhibition of presynaptic release of excitatory neurotransmitters (gabapentin, lamotrigine), and enhancing the activity of GABA receptors (topiramate). The most common adverse effects are impaired mental (somnolence, dizziness, cognitive impairment, fatigue) and motor (ataxia) function, which limit clinical use, particularly in elderly patients. Other serious side effects have been reported, including hepatotoxicity, thrombocytopenia, dermatologic and hematologic reactions.⁹⁴ Specific indications include trigeminal neuralgia for sodium- and diabetic neuropathy for calcium-channel blockers.⁹⁵

ANTIDEPRESSANTS

Antidepressants are used in the treatment of neuropathic pain and headache. They are divided into nonselective noradrenaline/5-HT reuptake inhibitors (amitriptyline, imipramine, clomipramine, duloxetine, venlafaxine), preferential noradrenaline reuptake inhibitors (desipramine), and selective 5-HT reuptake inhibitors (citalopram, fluoxetine). The reuptake block leads to a stimulation of endogenous monoaminergic pain inhibition in the spinal cord and brain. Tricyclic antidepressants also have NMDA receptor antagonist, endogenous opioid enhancing, Na^+ channel blocking, and K^+ channel opening effects, which can suppress peripheral and central sensitization. Block of cardiac ion channels by tricyclics can lead to arrhythmias. In patients with ischemic heart disease, there may be increased risk of sudden arrhythmia, and in patients with recent myocardial infarction, arrhythmia, or cardiac decompensation tricyclics should not be used at all. Tricyclics also block histamine, cholinergic, and adrenergic receptor sites. Adverse events of antidepressants include sedation, nausea, dry mouth, constipation, dizziness, sleep disturbance, and blurred vision.⁹⁴

TOPICAL ANALGESICS

The topical application of various analgesics is an area of considerable interest because many chronic pain syndromes

depend on the peripheral activation of primary afferent neurons.^{3,4} The localized administration can potentially optimize drug concentrations at the site of pain generation, while avoiding high plasma levels, systemic side effects, drug interactions, and the need to titrate doses into a therapeutic range. Studies have demonstrated effectiveness for topical NSAIDs, tricyclic antidepressants, capsaicin, local anesthetics, and opioids.^{4,94,96,97}

Topical NSAIDs are typical over-the-counter medications, widely advertised and used for acute and chronic pain. A large number of formulations (cream, gel, ointment) are commercially available. Meta-analyses concluded that topical NSAIDs have limited efficacy in chronic musculoskeletal pain.⁹⁶ Topically applied capsaicin interacts with nociceptive neurons via the TRPV1 receptor. It causes an initial activation of these neurons with release of substance P. This is perceived as a burning or itching sensation with a flare response and occurs in a high number of patients.⁹⁶ After repeated application desensitization occurs, probably due to depleting sensory neurons of substance P. Another potential mechanism is a direct toxic effect on small-diameter sensory nerve fibers. Topical capsaicin was shown to provide pain relief in postherpetic neuralgia, postmastectomy syndrome, osteoarthritis, and a variety of neuropathic syndromes.⁹⁸

Topical formulations of local anesthetics block Na^+ channels in primary afferent neurons. Blockade of Na^+ channels reduces impulse generation both in normal and in damaged sensory neurons. Such neurons exhibit spontaneous and ectopic firing, possibly contributing to certain conditions of chronic neuropathic pain. Under these conditions the altered expression, distribution, and function of ion channels along axons is associated with increased sensitivity to local anesthetics. Thus, pain relief may be achieved with local anesthetic concentrations lower than those that totally block impulse conduction.⁹⁹ Some studies using lidocaine patches and gels showed reduction of allodynia in postherpetic neuralgia and other types of neuropathic pain.⁹⁶

Topically applied or locally injected opioids produce analgesia by activating opioid receptors on primary afferent neurons. This leads to inhibition of Ca^{++} , Na^+ , and TRPV1 currents, which are activated by inflammatory agents.^{9,62} Subsequently the excitability of nociceptors, the propagation of action potentials, and the release of proinflammatory neuropeptides (substance P) from sensory nerve endings are inhibited. All of these mechanisms result in analgesia or antiinflammatory effects (or both).^{9,100} Other mechanisms accounting for the particular efficacy of peripheral opioids in pain associated with inflammation include upregulation¹⁰¹ and accelerated centrifugal transport of opioid receptors in sensory neurons,¹⁰² enhanced G-protein coupling of peripheral opioid receptors,¹⁰³ and disruption of the perineurial barrier facilitating access of opioid agonists to their receptors.^{104,105} Consistently, the perineural application of opioids along uninjured nerves (e.g., axillary plexus) does not reliably produce analgesic effects.¹⁰⁶ In addition, the production and secretion of endogenous opioid peptides from immune cells within injured tissue^{10,107} appears to produce additive/synergistic interactions¹⁰⁸ rather than tolerance at peripheral opioid receptors.¹⁰⁹ Peripheral opioid administration is regularly used and well documented

in the case of perioperative intraarticular morphine.¹¹⁰⁻¹¹¹ Intraarticular morphine also produces analgesia in chronic rheumatoid and osteoarthritis where its effect was shown to be similarly potent to standard intraarticular steroids and long lasting, possibly due to morphine's antiinflammatory activity.^{9,100} In numerous small studies, locally applied opioids (e.g., in gels) have shown analgesic efficacy in the treatment of skin ulcers, cystitis, cancer-related oral mucositis, corneal abrasion, and bone injury. No significant adverse effects have been reported.⁹⁷

OTHER ANALGESICS AND ADJUVANTS

Local anesthetics have been used orally, intravenously, in trigger-point injections, and in regional anesthetic techniques for selected chronic pain syndromes (see later under "Interventional Methods Used in Chronic Pain" and other chapters on "local anesthetics"). Their systemic application exhibited mixed success in various neuropathies. Meta-analyses indicate that local anesthetics produce moderate analgesic effects of questionable clinical significance in neuropathic pain.⁹⁴ Severe side effects including arrhythmias, dizziness, nausea, and fatigue limit the systemic application of local anesthetics.

α_2 -Adrenergic receptors are G-protein coupled and, similar to opioids, α_2 -agonists (clonidine) lead to opening of K^+ channels, inhibition of presynaptic Ca^{++} channels, and inhibition of adenylyl cyclase. Thus, like opioids, α_2 -agonists reduce neurotransmitter release and decrease postsynaptic transmission, resulting in an overall inhibitory effect.¹¹² Clonidine may exert analgesic effects in some neuropathic pain syndromes.⁹⁴ However, its systemic use is limited by sedation, hypotension, and bradycardia.

Cannabinoids have been studied extensively and are currently in the focus of public interest. Animal and *in vitro* models have shown that derivatives of tetrahydrocannabinol produce antinociceptive effects and that cannabinoid receptors and their endogenous ligands are expressed in pain-processing areas of the brain, spinal cord, and periphery. Peripheral cannabinoid receptors likely play a prominent role in pain inhibition.⁹ Meta-analyses of human studies concluded that the analgesic effects of cannabinoids are modest, not superior to those of other analgesics, and of questionable clinical significance. Psychotropic side effects, sedation, dizziness, cognitive impairment, nausea, dry mouth, and motor deficits are limiting factors in clinical practice.^{113,114}

Drugs reducing muscle spasm (e.g., benzodiazepines, baclofen) are often used in musculoskeletal pain but the available evidence does not indicate lasting beneficial effects while drowsiness and dizziness are frequently encountered.¹¹⁵ Baclofen activates GABA-B receptors pre-synaptically and post-synaptically, leading to a decrease in excitatory and an increase in inhibitory neurotransmission. In some reports it was found to exhibit analgesic effects in trigeminal neuralgia and central neuropathic pain. The most common side effects are drowsiness, dizziness, and gastrointestinal distress.¹¹⁶ Botulinum toxin inhibits acetylcholine release at the neuromuscular junction and may alleviate muscle spasticity. The use of botulinum toxin injections has produced inconsistent results in headaches and was not effective in myofascial trigger points, orofacial, or neck

pain.^{94,117,118} Side effects include pain and erythema at the injection site and unintended paralysis of adjacent muscles.

The synthetic peptide ziconotide blocks N-type voltage-sensitive Ca^{++} channels and thereby inhibits release of excitatory neurotransmitters from central terminals of primary afferent neurons in the spinal cord. It has been approved for intrathecal application but produces substantial side effects (dizziness, confusion, abnormal gait, memory impairment, nystagmus, hallucinations, vertigo, delirium, apnea, hypotension) and, thus, is suitable for only a small subset of patients with otherwise intractable pain.¹¹⁹ Under the assumption of antiinflammatory activity, steroid injections are frequently used epidurally or perineurally, albeit without convincing evidence for effectiveness (see the later section, "Therapeutic Nerve Blocks").

Antiemetics are used to treat nausea, a frequent side effect of analgesics (particularly opioids) and a frequent complaint in cancer patients. Recommendations for the treatment of postoperative nausea and vomiting cannot readily be extrapolated to the chronic pain patient. For example, in cancer patients, etiologies other than opioids have to be considered, such as radiotherapy and chemotherapy, uremia, hypercalcemia, bowel obstruction, and increased intracranial pressure. In addition, pain itself, as well as anxiety, can cause nausea. Management guidelines for the treatment of nausea and vomiting are available and the selection of antiemetics should be mechanism-based.^{67,120} The medullary chemoreceptor trigger zone, gastrointestinal stimulation or failure, vestibular and cortical mechanisms, as well as alterations of taste and smell, may contribute to nausea and vomiting, particularly in cancer patients. Most recommendations for the choice of antiemetic medication include gastrointestinal prokinetics (metoclopramide), phenothiazines (e.g., levomepromazine), dopamine receptor antagonists (e.g., haloperidol), serotonin antagonists (e.g., ondansetron), and antihistamines (e.g., cyclizine). In addition, the use of dexamethasone (unknown mechanism), anticholinergics (e.g., scopolamine), and neurokinin-1 receptor antagonists has been reported. Combinations of antiemetics with different modes of action can be used. Many of these drugs cause undesirable side effects by themselves (e.g., sedation, drowsiness, confusion, extrapyramidal symptoms).^{67,120} The efficacy of cannabinoids and benzodiazepines is considered comparatively low and they are not recommended as first-line treatment.^{120,121}

Laxatives are indicated when bowel movements are less than three per week, and are associated with difficulty or discomfort. Risk factors for constipation include opioid medication, older age, advanced cancer, hypokalemia, immobilization, as well as therapy with tricyclics, phenothiazines, anticonvulsants, diuretics, and iron supplements. Opioid-related constipation is mediated through intestinal and (partially) through central μ -receptors.⁶⁶ It is the most commonly occurring side effect of opioid medication in cancer patients and frequently does not exhibit tolerance. Ample fluid intake, fiber-rich nutrition, and mobilization are nonpharmacologic approaches to prophylaxis, but recommendations are mostly derived from anecdotal evidence.¹²² Laxatives include bulk forming, osmotic, and hyperosmolar agents; substances for colonic lavage; prokinetic drugs; and opioid antagonists. Recommendations usually include lactulose, senna, or polyethylene glycol

as a first choice.⁶⁷ However, lactulose should be avoided in patients with impaired fluid intake, such as the elderly and those with advanced cancer. If insufficient, the drugs of first choice may be combined with paraffin or anthraglycosides (bisacodyl). Rectal sorbitol or contrast medium are the choices for the next more intensified step. Prokinetic drugs, such as metoclopramide, are sometimes added for refractory constipation. A possible alternative in opioid-related constipation are opioid antagonists. To avoid central effects reducing analgesia or producing withdrawal, oral naloxone and the peripherally restricted antagonists methylnaltrexone and alvimopan were developed. Their use in clinical practice is limited by relatively low response rates, adverse effects, and high costs.¹²³

DEVELOPMENT OF NOVEL ANALGESICS

Areas of intense research and examples emerging as potential drug targets include calcitonin-gene-related-peptide, Na^+ channels expressed in peripheral nociceptive neurons ($\text{Na}_v1.8$, $\text{Na}_v1.7$), voltage-gated Ca^{++} channels (e.g., $\text{Ca}_v2.2$), antibodies against nerve growth factor, the capsaicin receptor TRPV1, and the P2X receptors.²¹ Increasing attention is paid to augmentation of endogenous opioid and cannabinoid mechanisms, to (biased) opioid receptor signaling, and to the activation of peripheral opioid receptors to avoid central side effects.^{11,62-64,124,125} However, failures in clinical phases of analgesic drug development are common and have been attributed to inappropriate animal models or nociceptive tests, species differences, publication bias, lack of mechanistic understanding, shortcomings in experimental design, randomization, blinding, and statistical analysis.²¹

Interventional Methods used for Chronic Pain

The popularity of interventional methods has decreased over time. While early pain therapists (e.g., Leriche) were generally using “blocks” to treat pain, the biopsychosocial concept of chronic pain has led to a much more cautious and judicious use of such techniques (see earlier section, “Interdisciplinary Management of Chronic Pain”), particularly since most of these are not evidence-based. Block therapy alone is usually not curative, but it can facilitate participation in rehabilitation and therefore does have a role in the management of chronic pain. Regardless which procedure is considered, a consensus decision on its use has to be reached within the interdisciplinary team.

DIAGNOSTIC NERVE BLOCKS

Neural blockade is thought to be a useful tool to better understand the mechanisms underlying pain in an individual patient and to provide a prognosis for planned neuroablative procedures (particularly in cancer pain). Differential blockade aims to selectively block either single peripheral nerves to identify an anatomical pain source, or to selectively block only one type of nerve fiber (autonomic vs. somatic).¹²⁶ However, the clinical usefulness of these procedures could not be confirmed.^{127,128} In particular, the

validity of diagnostic nerve blocks is limited by the complexity of factors determining pain perception (see above section, “Biopsychosocial Concept of Pain” and “Interdisciplinary Management of Chronic Pain”). Furthermore, the assumption that local anesthetics can selectively produce conduction block of only one fiber type in a nerve is probably false.¹²⁶ Nevertheless, experienced and observant clinicians have found that such procedures may occasionally provide information that is helpful in guiding subsequent therapy, although systematic reviews had methodological limitations.^{129,130}

THERAPEUTIC NERVE BLOCKS

Cancer Pain

Therapeutic nerve blocks are used only in a minority of patients with cancer-related pain. Here, interventional treatment represents the fourth step in the World Health Organization analgesic ladder.¹³¹ About 90% to 95% of patients usually obtain adequate pain relief from pharmacologic management.¹³² A comprehensive biopsychosocial approach to pain management—as in chronic noncancer pain—and carefully balancing risks against benefits in individual patients are prerequisites for successful use of interventional techniques.¹³³ Therapeutic nerve blocks extend the treatment range when conservative methods fail to achieve tolerable pain or side-effect levels (or both). For example, neuropathic, incidental, or breakthrough pain are sometimes poorly controlled by systemic analgesics and may be indications for invasive therapy. Well evaluated interventional techniques like celiac plexus block, hypogastric plexus block, and saddle blocks should not be withheld from cancer patients in a palliative symptom control context.¹³⁴

Sites for neurolyses are intercostal nerves (e.g., in rib metastasis), the superior hypogastric ganglion, the ganglion impar, and the lumbar sympathetic ganglia (e.g., for pelvic tumors). In perineal pain due to local infiltration of rectum cancer, intrathecal neurolysis may be considered if bladder and sphincter function are not of concern.^{134,135} An indication for thoracic intrathecal or epidural neurolysis might be advanced lung cancer.¹³⁶ As a neurolytic agent, alcohol may be preferred due to its perceived higher success rate and longer duration of pain relief (3-6 months) compared to phenol (2-3 months), although no studies directly comparing these two agents are available. The limited period of pain reduction and the limited possibility of repeat injections are reasons why neurolysis is mostly used in patients with short life expectancy.¹³⁷

Non-Cancer-Associated Pain

Both the complexity of factors contributing to pain perception and perpetuation (see earlier in sections “Biopsychosocial Concept of Pain” and “Interdisciplinary Management of Chronic Pain”) and the detrimental long-term effects of nerve destruction (neuropathic pain caused by spontaneous ectopic neuronal discharges, upregulation of neuronal ion channels, and excitatory amino acid receptors, see earlier in sections “Physiological Changes in Persistent Pain” and “Antiepileptic Drugs”) caution against neuroablative procedures in the noncancer patient. Nonetheless, many practitioners advocate radiofrequency ablations or

cryoneurolysis at facet joints, sacroiliac joints, and other destructive procedures. However, the IASP makes no conclusive recommendations due to the poor quality of available data.¹³⁸

Nondestructive procedures include trigger point, epidural, perineural, and intraarticular injections of local anesthetics, or steroids (or both). Steroids are used under the assumption of antiinflammatory activity. For example, in chronic back or neck pain (the most common patient complaints), injections into facet (or zygapophyseal) joints or along the medial branch from the posterior ramus of the spinal nerve root are frequently performed, however, without convincing documented long-term results.^{139,140} Similarly, injections into sacroiliac joints, trigger points, or occipital nerve blocks show no consistent long-lasting effects.^{129,141,142} Epidural steroids are also used extensively for low back and neck pain,¹⁴³ but they provide questionable long-term pain relief in RCTs.¹⁴⁴ The same applies to lumbar transforaminal epidural steroid injections.¹⁴⁵ Thus, the described invasive procedures should be limited to acute pain states in patients without biopsychosocial risk factors for chronicification of pain, and only as an element within a physical rehabilitation or multimodal treatment program.¹⁴⁶ Sympathetic nerve blocks with local anesthetics, often carried out as a series, such as in herpes zoster-associated pain and complex regional pain syndrome, are commonly used but evidence from RCTs is lacking.¹⁴⁷ Anecdotal reports have described sympathetic blocks for ischemic pain, such as in peripheral vascular or Raynaud disease.

CONTINUOUS CATHETER TECHNIQUES

Continuous drug delivery to the intrathecal or epidural space can be accomplished via programmable implanted pumps, implanted accessible reservoir systems, and tunneled exteriorized catheters. The principal benefit appears to be the reduction of systemic side effects. As with nerve blocks, the evidence of effectiveness of these approaches is stronger for cancer pain than for chronic nonmalignant pain.

Cancer Pain

Only a small minority of cancer patients require neuraxial (intrathecal, epidural) drug delivery due to intolerable side effects, but in patients refractory to systemic analgesics, such methods may be underused.^{148,149} The preponderance of evidence supporting this mode of drug delivery is derived from nonrandomized, uncontrolled studies.^{150,151} The advantage of the neuraxial technique is its ubiquitous availability in most anesthesia departments, but disadvantages are the chance of inhomogeneous distribution of the analgesics, possible systemic absorption, and limited duration of therapy due to local granuloma formation and technical failures.¹⁵¹ Usually, morphine (1-15 mg, dependent on preceding systemic dosage) or hydromorphone are recommended as drugs of first choice for intrathecal catheter analgesia. For refractory pain, combinations with bupivacaine, clonidine, ziconotide, and other compounds have been used.¹⁵⁰

Non-Cancer-Associated Pain

No RCTs are available, but a number of observational reports describe continuous catheter techniques for chronic

noncancer pain.¹⁵¹ Most of these studies used intrathecal morphine, and some hydromorphone, baclofen, or ziconotide in patients with chronic low back pain. On average, these patients exhibited increasing daily morphine doses over time, and a high incidence (up to 25%) of complications, such as catheter obstruction, catheter-tip granuloma formation, pruritus, urinary retention, and infection. Effectiveness of these techniques in relieving pain or improving function compared to placebo, natural history, or other treatments has not been shown¹⁵¹ or is limited.¹⁵²

STIMULATION TECHNIQUES

Stimulation techniques frequently used in pain management include acupuncture, spinal cord (or dorsal column) stimulation (SCS), and transcutaneous electrical nerve stimulation (TENS). Acupuncture has been popular among patients for a long time and lately also within the medical community. Systematic reviews of sham-controlled studies in migraine prophylaxis and arthritic pain showed that using traditional Chinese concepts of meridians and specified classic points are as effective as the selection of acupuncture points at random.^{153,154} There is inconclusive evidence that acupuncture may be of benefit in osteoarthritis^{154,155} and chronic low back pain.¹⁵⁶⁻¹⁵⁸ SCS has gained new interest with the introduction of the high-frequency technique,¹⁵⁹ but its superiority still has to be demonstrated.¹⁶⁰ So far SCS has not been validated by adequately powered and blinded RCTs in chronic pain.^{161,162} Unblinded studies suggest that selected patients with complex regional pain syndrome or back pain, especially with failed back surgery syndrome, might benefit from SCS, but controlled trials are needed.^{138,163}

Perioperative Management of Patients with Chronic Pain

CHARACTERISTICS OF CHRONIC PAIN PATIENTS IN THE PERIOPERATIVE PERIOD

In chronic pain patients, central sensitization or reduced endogenous inhibition may result in increased and prolonged pain after surgery.¹⁶⁴ Altered opioid sensitivity due to long-term exposure to opioid medications also has to be considered.¹⁶⁵ In addition, chronic pain patients may exhibit higher preoperative expectation of pain, anxiety, depression, or hypervigilance.^{166,167} It may be difficult to distinguish normal from maladaptive anxiety, but patients with cancer pain are more likely to be anxious than cancer patients without pain. In addition, the chronic pain patient, including the patient with cancer, is not as confident of recovery as other patients with chronic diseases.¹⁶⁸ Thus, difficult perioperative pain control and, possibly, an increased risk of chronic pain development after surgery have to be expected. However, chronic pain patients, with or without long-term opioid medication, opioid abuse or misuse, require and must receive adequate pain control.

The preanesthetic visit should therefore include questions regarding chronic pain and regular use of analgesics and adjuvant medication (also see Chapter 31). Although a number of characteristics including increased opioid

BOX 51.1 Risk Factors in the Perioperative Management of the Chronic Pain Patient

- Conventional perioperative analgesia regimens do not meet the needs of the chronic pain patient.
- Unrelieved postoperative pain due to undermedication may provoke withdrawal.
- Patients tend to underreport their medication.
- With uncontrolled anxiety or fear of pain, patients tend to overestimate the effect of painful stimuli.
- Epidural and intravenous (IV) opioid (including patient-controlled analgesia [PCA]) requirements can be 2-4 times higher in opioid-consuming than in opioid-naïve patients.
- Expect prolonged recovery and need for postoperative analgesia.
- Anxiety and insufficient coping result in poor compliance with analgesic strategies.
- Individual variations in response to opioids may necessitate selection of the optimal drug and dosing by sequential trials.
- Individual titration of doses to find the optimal balance between analgesia and adverse effects is required.
- Adjuvant medication may interfere with anesthesia and postoperative analgesia.

Adapted from Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59-76.²⁰²

demand, underreporting of pain, and noncompliance are known, only few specific recommendations are available, such as adequate increase of opioid dose for analgesia, continuation of preoperative analgesics to prevent withdrawal, and intensive education to strengthen the patient's coping potential. No differences between specific techniques for postoperative analgesia (e.g., systemic, patient-controlled, or regional analgesia) have been demonstrated so far. Furthermore, preoperative intensity of pain alone, independent of the use of analgesics, correlates positively with postoperative pain.¹⁶⁹ Chronic pain patients often suffer from prolonged inactivity or neurologic deficits (or both), which increase the risk for adverse events during the perioperative period. Some key issues are summarized in **Box 51.1**.

CHRONIC USE OF ANALGESICS AND ADJUVANT DRUGS

Chronic pain patients are often pretreated with opioids, COX inhibitors, antidepressants, or anticonvulsants (or combinations). Tolerance, drug interactions, and side effects may occur. In addition, inappropriate or excessive medication is commonly observed.^{47,170} Chronic pain patients tend to underestimate and underreport their medication use.¹⁷¹ Thus, undertreatment in the perioperative period may be unnoticed and may induce a neuroexcitatory withdrawal syndrome and associated cardiopulmonary strain.

Chronic opioid medication has been discussed thoroughly in the literature (see earlier in section "Opioids"). Together with aggressive marketing, this has gradually led to decreasing reservations among practitioners toward the use of these drugs. As a result, opioids are used more frequently in both cancer and noncancer pain patients and the majority of the latter are now prescribed opioid medication.^{47,170}

While this seems justified in cancer pain, opioids are usually not indicated in chronic noncancer pain (see earlier section "Opioids"). Nevertheless, anesthesia providers are increasingly confronted with patients receiving long-term opioid treatment. Such pretreatment can result in several-fold increased and prolonged requirement for systemic and epidural analgesics in the perioperative period compared to opioid-naïve patients.^{73,172-174} Chronic pain patients with prior opioid consumption may also exhibit higher postoperative pain scores.¹⁷⁴ The increased postoperative analgesic demands may be due to lower pain thresholds or to a need for higher drug concentrations. In addition, opioid requirements can be influenced by gender, genetic predisposition, age, type of surgery, and preoperative pain levels.^{74,169} On the other hand, opioid-related side effects (e.g., nausea and pruritus) may be less dominant. Physicians and nurses may overestimate tolerance, addiction, and sedation, but underestimate dependence. A paramount concern is the maintenance of adequate perioperative opioid dosing to prevent withdrawal (see **Box 51.1**).^{173,174}

COX inhibitors are the most commonly used nonopioid analgesics. They produce serious side effects in the gastrointestinal tract, kidneys, cardiovascular and coagulation systems (see earlier section "Drugs Used for Chronic Pain"). Major concerns for the anesthesiologist are coagulation disturbances, renal impairment, and the increased risk for hematoma formation associated with spinal and epidural anesthesia.

Antiepileptic drugs can interfere with anesthesia in different ways. Sedation produced by anticonvulsant drugs may have additive effects with anesthetics, whereas drug-induced enzyme induction could alter responses to or contribute to the organ toxicity of anesthetics. Gabapentin has a favorable side effect profile, and its relative absence of drug interactions allow continuation and rapid titration in the perioperative period.¹⁷⁵ Phenytoin and carbamazepine accelerate recovery from nondepolarizing muscle relaxants, but the mechanism is unclear. Preoperative exclusion of toxic serum levels of phenytoin is recommended to reduce the risk of atrioventricular conduction block. States of disorientation, nystagmus, ataxia, and diplopia may be manifestations of excessive plasma concentrations. Carbamazepine may produce sedation, ataxia, nausea, and (rarely) bone marrow depression or hepatorenal dysfunction. Plasma sodium levels have to be monitored perioperatively to avoid hyponatremia. Oral valproic acid is commonly used for prophylaxis of migraine and intravenous valproic acid may be used to control episodic headaches.¹⁷⁶ It may inhibit activity of hepatic microsomal enzymes and interfere with platelet aggregation.¹⁷⁷ Antiepileptics should never be discontinued abruptly to avoid central nervous system hyperexcitability. Stable dosages need to be maintained throughout the perioperative period.

Antidepressants are frequently used for neuropathic pain and for associated depression. Adverse effects are numerous and include sedation, anticholinergic effects, and cardiovascular changes. Electrocardiographic changes, such as prolongation of PR-interval and widening of the QRS complex, can occur but previous suggestions of increased risk of perioperative cardiac dysrhythmias have not been substantiated in the absence of drug overdose.¹⁷⁸ Therefore, antidepressants need not be discontinued before anesthesia, but

increased anesthetic requirements may be expected due to enzyme induction. Postoperatively, the likelihood of delirium and confusion may be increased as a result of additive anticholinergic effects. Selective serotonin reuptake inhibitors and atypical antidepressants like mirtazapin or venlafaxine are less likely to interfere with anesthesia.

Ketamine is a mixed opioid agonist/NMDA antagonist that can produce analgesia at subanesthetic doses in selected patients with neuropathic pain.^{179,180} Very rarely, patients taking oral ketamine medication on a chronic basis will be encountered. In these cases, perioperative administration of ketamine should be discontinued because correct conversion from oral to intravenous ketamine is difficult.¹⁸¹ Within analgesic dose ranges, the risk of a withdrawal syndrome is small.^{180,182}

Benzodiazepines are not analgesic and are rarely used in chronic pain, with the exception of palliative care situations.^{115,183} Nevertheless, since chronic pain is a predictor of increased benzodiazepine use, this should be explored in the preanesthesia visit.¹⁸⁴ Side effects relevant to anesthesia include sedation and skeletal muscle weakness. Due to their long half-life, delayed withdrawal should be anticipated and avoided by maintaining stable perioperative dosage. Neuroleptics are also inappropriate, but sometimes used in chronic pain.¹⁸⁵ In the perioperative period, patients treated with antipsychotic drugs can develop a neuroleptic malignant syndrome. Hyperthermia, hypertonicity of skeletal muscles, fluctuating levels of consciousness, and autonomic nervous system instability are typical symptoms.

DEPENDENCE, ADDICTION, AND PSEUDOADDICTION

Physical dependence is defined as a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be elicited by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, or administration of an antagonist.¹⁸⁶ Dependence is not synonymous with tolerance (see earlier section “Opioids”). All opioids, benzodiazepines, and anticonvulsants produce clinically relevant physical dependence when administered for a prolonged period of time, but sometimes physical dependence can develop within hours of agonist exposure.⁷¹ Thus, all patients with continuous preoperative opioid intake should be considered at risk for withdrawal syndrome if adequate substitution of opioids in the perioperative period is withheld. Opioid and benzodiazepine withdrawal syndromes, especially tachycardia and hypertension, may be detrimental for the high-risk cardiac patient. Rapid withdrawal from anticonvulsant drugs may trigger seizures, anxiety, and depression.

Addiction is a behavioral syndrome characterized by evidence of psychological dependence (craving), uncontrolled/compulsive drug use despite harmful side effects, and other drug-related aberrant behavior (e.g., altering prescriptions, manipulating healthcare providers, drug hoarding or sales, unsanctioned dose escalation).^{186,187} The prevalence of opioid addiction is up to 34% in patients with chronic nonmalignant pain and about 8% in patients with cancer pain.^{187,188} Special considerations in the management of the drug-addicted patient are discussed elsewhere.^{173,174,189}

MANAGEMENT AND PRACTICAL RECOMMENDATIONS

Perioperative management has to address the risk of opioid withdrawal, the altered pain sensitivity, and the psychological alterations typical in the chronic pain patient population. Most of the following recommendations have to be considered as “expert views” only.^{174,190,191}

Preoperative Evaluation (also see **Chapter 31**)

Preanesthesia evaluation is necessary to educate patients, to organize resources for preoperative improvement of the patient’s physical function, to choose optimal anesthetic techniques, and to formulate plans for postoperative recovery, including perioperative pain management.¹⁷³ Misconceptions about the surgical procedure, the role of the anesthesiologist in perioperative care, and postoperative pain treatment are common among patients.¹⁹² A thorough history must be obtained to identify all preoperative medications, including opioids, other analgesics and adjuvants, as well as signs of psychiatric comorbidity and aberrant drug-related behavior. Patients with spinal cord stimulators should be instructed to turn off the device. Screening tools and thorough education of the patient are recommended.^{167,193} Consultation of a pain specialist should always be considered. Pertinent issues and practical recommendations are summarized in Boxes 51.1 and 51.2.

Perioperative Management

To avoid opioid withdrawal, the preoperative systemic dosage should be continued throughout the perioperative period and mixed agonist/antagonists (buprenorphine, nalbuphine) must be avoided. If a neuraxial catheter with opioid medication is used, the flow and concentration of the opioid should be continued throughout the perioperative period as background analgesia.¹⁹⁴ For minor and medium surgery, oral slow-release opioid medication may be continued at its regular intervals. For major surgery with postoperative restriction of enteral intake, oral opioids should be discontinued and replaced by equivalent doses of intravenous opioids, which have to be continued for the entire perioperative period. This applies to general as well as regional anesthesia. The anesthesia technique should be selected on an individual basis considering the patient’s expectations since no data are available favoring general, regional, or combined anesthesia for this patient population.¹⁹¹ The frequency and extent of monitoring techniques should be adapted to the risk of patient instability.

Individually adapted regimens are usually superior to “conventional” analgesia, regardless of the specific analgesia technique used.¹⁹⁵ In minor and medium surgery, an opioid/NSAID combination should always be considered to enhance opioid effects. Since pregabalin and gabapentin can reduce postoperative pain and opioid consumption¹⁹⁶ and have anxiolytic effects,¹⁹⁷ the chronic pain patient with anxiety might benefit. A dose range of 150 mg BID until the second or third postoperative day has been recommended.¹⁹⁰ Ketamine may also be applied as an adjunctive therapy,¹⁸⁰ but there are no data to encourage its routine use for the chronic pain patient in the perioperative period. Support from a multimodal pain treatment facility or the acute pain service should be requested. Apart from the

BOX 51.2 Preoperative Considerations and Recommendations in Patients With Chronic Pain

- Take thorough history to identify all analgesic and adjuvant medications, risk factors, and comorbidity.
- Educate the patient about the perioperative procedures, the potential for aggravated pain, and increased opioid requirements.
- Communicate plans between the designated anesthesiologist in the operating room, the postanesthesia care unit, and the surgical and nursing personnel on the ward.
- Differentiate between addiction, pseudoaddiction, and physical dependence in patients on long-term opioid medication.
- Expect physical dependence in patients on long-term opioid medication.
- Continue previous long-acting opioid analgesics for short procedures.
- For major surgery calculate and order background infusion of an equianalgesic opioid dose for patients with NPO for >8 h to be started in the OR.
- Order regular opioid medication on the morning of surgery.
- Maintain anticonvulsant drugs and benzodiazepines at preoperative doses.
- Discontinue all other adjuvants if NPO status remains >24 h.
- Identify untreated depressive disorder with screening questions for disturbed sleep, lowered mood, reduced concentration, self-confidence, and motivation.
- Identify untreated anxiety disorder with screening questions for restlessness, irritability, difficulties to control anxiousness, and worrying.
- Consider referral to pain specialist for evaluation.
- Choose regional or general anesthesia based on individual considerations.

OR, Operating Room.

Adapted from Farrell C, McConaghay P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148; and Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59–76. ^{191,202}

choice of analgesia technique and adequate opioid medication, optimization of organizational structures is a key factor for improving perioperative analgesia.¹⁹⁸ If addiction is suspected the patient should be re-evaluated for weaning or rehabilitation only after recovery from surgery and postoperative pain.¹⁹⁹ Specific risk factors in chronic pain patients are summarized in Box 51.1.

Postoperative Regional Anesthesia

Although there is no strong evidence indicating superiority of particular anesthetic techniques for postoperative analgesia in chronic pain patients, individual considerations may favor regional anesthesia, particularly because these patients are prone to intensified postoperative pain experiences. Chronically opioid-consuming patients need their daily systemic dosage by the intravenous or oral route to prevent withdrawal.¹⁷³ In addition, postoperative analgesia with an epidural or plexus catheter may be accomplished with a combination of local anesthetics and opioids, similar to patients without chronic pain (see

Chapters 45 and 46). However, higher doses of epidural opioids are recommended since cross-tolerance between orally and epidurally administered opioids has been described. Epidural lipophilic opioids (fentanyl, sufentanil) may provide better postoperative pain relief than epidural morphine in chronically opioid-consuming patients, which has been attributed to the need of a lower receptor occupancy or incomplete cross-tolerance between morphine and sufentanil.²⁰⁰

Postoperative Intravenous Opioids

The total required opioid dose consists of the daily dose taken before and the dose made necessary by surgical stimulation. A continuous perioperative intravenous opioid infusion equivalent to the regular daily dosage is recommended if the oral route is unavailable.^{173,195} Additional bolus doses of opioid or nonopioid analgesics (or both) have to be titrated to individual needs to achieve adequate pain control in the postanesthesia care unit. Depending on the local circumstances, this may be patient-, nurse- or physician-controlled. The bolus size should be equal to the hourly dose of the background infusion. Once the patient demands less than four extra bolus doses per day, the background infusion may be reduced in daily steps of about 20% to 30%. For calculation of opioid dose equivalents, the relative potency, half-life, bioavailability, and route of administration have to be considered.²⁰¹ As soon as possible, oral medication should be resumed. Intravenous doses during the first 24 to 48 hours after surgery should be converted to oral dose equivalents. Half of the total dosage may be delivered as long-acting and half as short-acting breakthrough medication for on-demand use.¹⁷³

Perioperative Transdermal Opioids

Transdermal fentanyl patches are relatively reliable in administering controlled amounts of the drug to the circulation over long periods. However, during surgery the amount of drug delivered to the patient may significantly shift. Changes in intravascular volume, body temperature, and volatile anesthetics alter skin permeability and perfusion resulting in relatively large fluctuations in transdermal fentanyl passage. In addition, forced-air warming blankets and heat packs applied onto the patch itself can lead to several-fold increases in fentanyl permeation through the skin.⁷³ Thus, in major surgery, removal of transdermal systems is advisable to avoid unforeseen decreases and increases of systemic opioid uptake. The transdermal opioid dose should be converted to intravenous morphine to be administered as a continuous background infusion.²⁰¹ Pertinent issues and practical recommendations are summarized in Box 51.3.

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BOX 51.3 Intra- and Postoperative Management Issues and Practical Recommendations

- Start background opioid infusion immediately when patient arrives in the OR.
- Remove opioid patch when major surgery is planned; in minor surgery patch may be continued without background infusion.
- Every chronic pain patient has to be seen postoperatively to evaluate pain at rest, pain with exercise (e.g., coughing), nausea, sedation, mobilization, and sleep quality.
- Monitor closely for signs of respiratory depression and of withdrawal (e.g., unexplained tachycardia, restlessness, sweating, confusion, hypertension).
- Integrate the patient in the acute pain service protocol if available.
- Titrate short-acting opioid for acute pain with 2-4 times the usual starting dose needed for an opioid-naïve patient.
- Add COX inhibitors, anticonvulsants, other adjuvants as needed.
- Evaluate demand-delivery-ratio of PCA frequently, adapt demand-dose in relation to background infusion (demand-dose equals hourly dose of background infusion).
- Increase background infusion in PCA in relation to the cumulative daily opioid demand dose (add 50%-75% of the daily demand-dose to background infusion).
- Change technique of postoperative analgesia if inadequate use persists in spite of repeated patient education.
- In case of insufficient epidural analgesia with morphine, use epidural fentanyl or sufentanil.
- In case of IV opioid dose escalation consider spinal/epidural opioid application or switch IV agonist.
- Reduce daily opioid doses after the second postoperative day stepwise to the preexisting dose.
- Switch back to oral or transdermal medication as early as possible; use 50%-75% of last daily IV opioid dose as slow release oral or transdermal delivery plus the rest as demand dose.
- When switching back to transdermal route consider 12-16 h delayed effects and supply patient for this period with sufficient on-demand analgesia.
- Do not attempt to solve a chronic pain problem in the immediate postoperative period.
- Use non-pharmacological techniques (distraction, relaxation) where appropriate and offer counselling in the pain unit after postoperative recovery.

COX, cyclooxygenase; IV, intravenous; OR, Operating Room; PCA, patient-controlled analgesia.

Adapted from Farrell C, McConaghay P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148; and Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59-76.^{191,202}

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KEY POINTS

- Palliative care is an interprofessional approach to symptom management and decision making for patients with a wide range of serious illnesses and is not limited to patients who are imminently expected to die.
- Palliative care teams reduce costs and decrease the burden of symptoms for patients with serious illnesses.
- Physicians receive limited training in discussing difficult topics and tend to focus on details and use medical jargon in conversations with seriously ill patients.
- Patients and families want physicians to be truthful and empathetic and to participate in shared decision making.
- While patients and families desire a prognosis, they understand and accept that physicians have difficulty prognosticating the future for an individual patient.
- Opioids administered in small doses are effective in treating dyspnea and do not hasten death in patients receiving palliative care.
- The presence of treatment limitations should prompt a thorough discussion of the perioperative plan between the patient and the surgical team.

What Is Palliative Medicine?

DEFINITION

The World Health Organization (WHO) defines palliative care as “an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”¹ Importantly, palliative care does not necessarily need to be limited to the end of life. The Center to Advance Palliative Care states, “unlike hospice care, palliative care can be provided at the same time as curative treatments; it is appropriate at any age and at any stage of a serious illness.” Illness has many facets; symptom management, family support, and aid in decision making are common areas of focus for palliative care teams (Fig. 52.1).² Symptom management encompasses physical symptoms (i.e., pain, constipation, nausea and vomiting, and delirium) as well as emotional symptoms (i.e., depression, anxiety, and distress). Palliative care refers to the work of an interprofessional team, whereas palliative medicine refers to the medical subspecialty focused on providing symptom relief and decision-making support for patients with serious illnesses.

PRIMARY VERSUS SPECIALIST PALLIATIVE MEDICINE

There is a distinction made among the levels of palliative care: primary versus specialist. This distinction facilitates the differentiation among the skills expected from all physicians, including anesthesiologists, and from those more suitable to a specialist service. Examples of primary palliative

medicine include basic pain and symptom management, as well as discussions about prognosis, goals of treatment, and resuscitation status.³ Specialty palliative medicine includes the management of refractory or complex symptoms, as well as the facilitation of conflict resolution among families, staff members, and treatment teams related to the goals of care (Fig 52.2).⁴

HISTORY OF PALLIATIVE MEDICINE

The word *palliative* comes from the Latin word *to clothe* and refers to the “covering up” of symptoms such as pain. Modern palliative medicine grew out of the hospice movement started by Dr. Cicely Saunders in the late 1960s,⁵ and introduced in the United States in the 1970s. Since that time, the field has broadened from a focus on patients at the end of life to include patients with serious illnesses. There is also growing recognition that many hospice principles, such as the relief from suffering, apply to all patients regardless of prognosis (Fig. 52.3).⁶ To meet this growing need, several academic medical centers have organized inpatient palliative care teams over the past decades.⁷

Currently, 90% of hospitals with more than 300 beds and 67% of hospitals with 50 or more beds have palliative care teams.⁸ Hospice and palliative medicine became a recognized subspecialty in 2006, with the first board examinations offered in 2008. Physicians from 10 medical specialties, including anesthesiology, are eligible to complete a fellowship and take the board examination.⁹ Between 2008-2017, 125 anesthesiologists were also certified in hospice and palliative medicine.¹⁰ There are now over 7600 hospice and palliative medicine physicians in the United States, and 1% to 2% of graduating

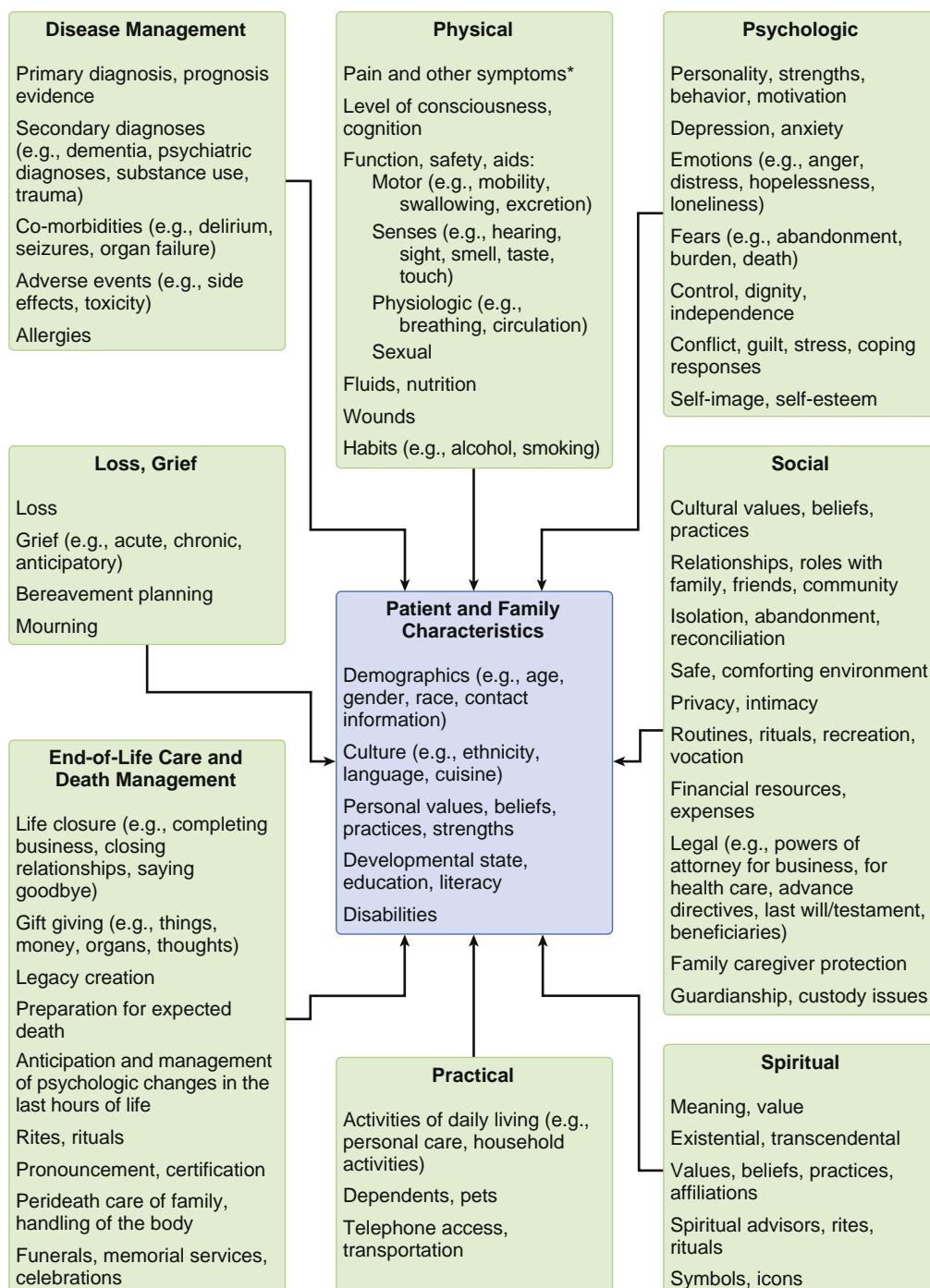


Fig. 52.1 Aspects of illness. *Other common symptoms include, but are not limited to: Cardiorespiratory: breathlessness, cough, edema, hiccups, apnea, agonal breathing patterns Gastrointestinal: nausea, vomiting, constipation, obstipation, bowel obstruction, diarrhea, bloating, dysphagia, dyspepsia Oral conditions: dry mouth, mucositis Skin conditions: dry skin, nodules, pruritis, rashes General: agitation, anorexia, cachexia, fatigue, weakness, bleeding, drowsiness, effusions (pleural, peritoneal), fever/chills, incontinence, insomnia, lymphedema, myoclonus, odor, sweats, syncope, vertigo (Modified from Ferris FD, Balfour HM, Bowen K, et al. A model to guide patient and family care: based on nationally accepted principles and norms of practice. *J Pain Symptom Manage*. 2002;24:106–123.)

hospice and palliative care fellows each year are from anesthesiology.^{10a,b}

WHY IS PALLIATIVE MEDICINE NEEDED?

The combination of an aging population and medical advancement has contributed to an increase in the number of patients with chronic illnesses. In the United States, Medicare

expenditures currently exceed \$600 billion, with 42% of Medicare expenses going to 5% of patients.¹¹ Many of these patients have multiple comorbidities, repeated or prolonged hospitalizations, or a life expectancy of less than 1 year, which make many of them appropriate for hospice or palliative care services.¹²

Patients with serious illnesses have a significant symptom burden, most often involving pain, dyspnea, anxiety, and

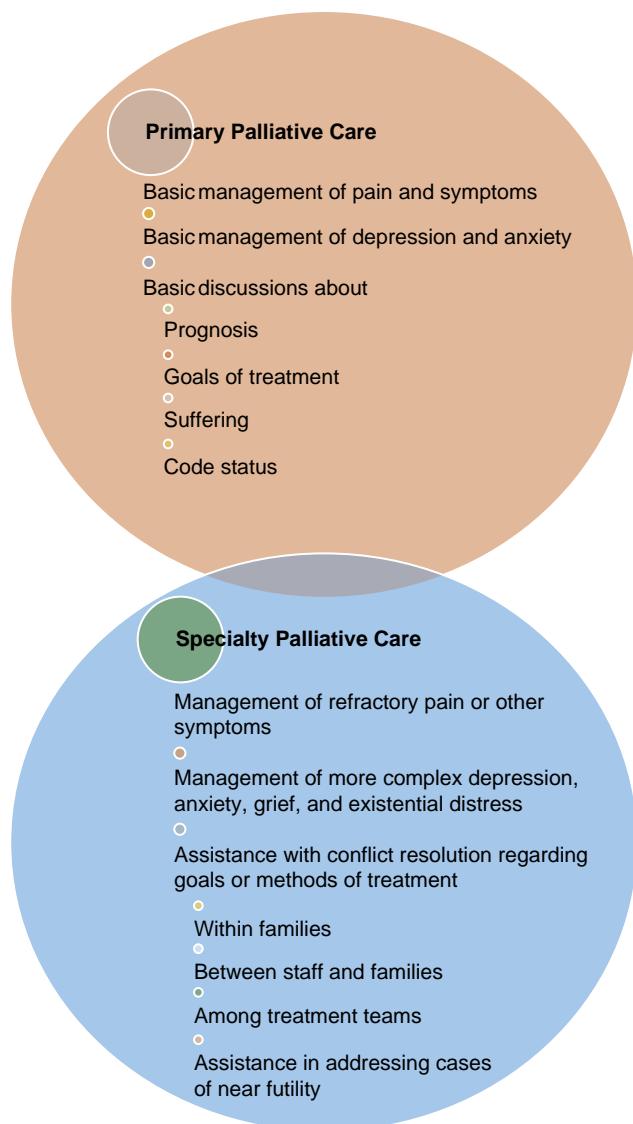


Fig. 52.2 Representative skill sets for primary and specialty palliative care. (Modified from Quill TE, Abernethy AP. Generalist plus specialist palliative care—creating a more sustainable model. *N Engl J Med*. 2013;368:1173–1175.)

depression, and their family members report similar concerns.¹³ Pain control during a life-limiting illness is often a major concern for patients and their families, and unfortunately, several surveys have found that they are often dissatisfied with the quality of pain control.^{13,14} Patients and families also describe poor communication with health professionals, particularly in the setting of conversations regarding prognosis.¹⁵ Palliative care, with its emphasis on symptom management and goal setting, attempts to address these concerns.

WHY IS PALLIATIVE MEDICINE IMPORTANT TO ANESTHESIOLOGISTS?

As patients who are older and more seriously ill undergo surgery,¹⁶ anesthesiologists should develop an understanding of the concepts of palliative medicine. Anesthesiologists have specific skills in symptom management that may benefit the patient, and they have a unique perspective on the surgical process that can provide insight to palliative medicine and surgery teams.¹⁷ As more patients and families interact with palliative care teams, anesthesiologists should be able to discuss related concerns and to develop an anesthetic plan that includes palliative concepts, including goals of care discussions and symptom management. Additionally, many pain and critical care anesthesiologists develop this specific expertise through their frequent management of seriously ill patients.

GLOBAL PALLIATIVE CARE

Approximately one half of the countries in the world have at least one hospice or palliative care service, although most exist in larger and more developed countries. Methods and locations of palliative care delivery are widely variable throughout the world, depending on the country's infrastructure. The variation in availability is vast, from 1 physician for every 1000 inhabitants in the tiny country of Niue near New Zealand to 1 per 8.5 million inhabitants in China and 1 per 90 million in Pakistan.¹⁸ The access to appropriate medications is often restricted and variable as well. An estimated 80% of people with pain worldwide are unable to access opioids, due to concerns about addiction or restrictive

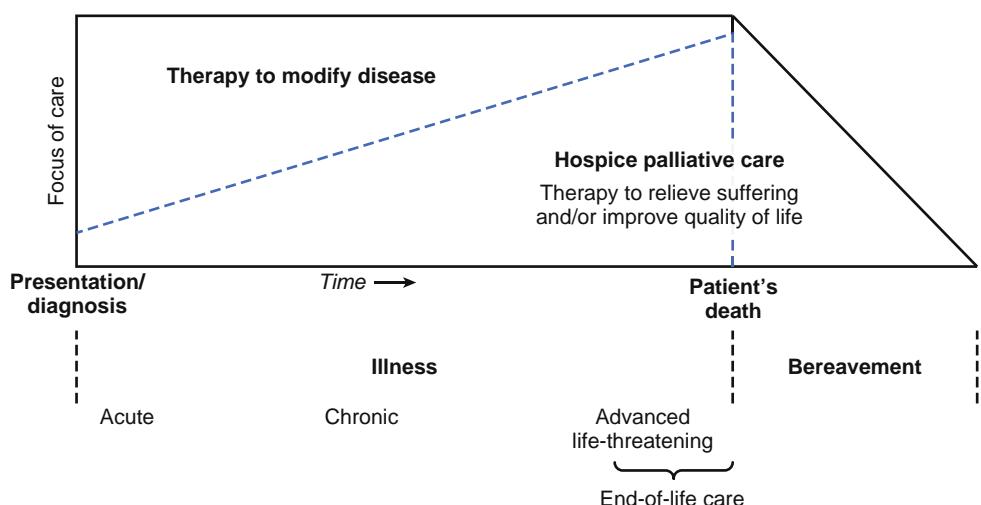


Fig. 52.3 Schematic illustration depicting the role of hospice care and palliative care during illness and bereavement. (From Ferris FD, Balfour HM, Bowen K, et al. A model to guide patient and family care: based on nationally accepted principles and norms of practice. *J Pain Symptom Manage*. 2002;24:106–123.)

national opioid policies.¹⁹ The WHO has implemented a “Public Health Strategy for Palliative Care” that incorporates aspects of policy, drug availability, and education to customize and integrate palliative care throughout the globe.²⁰

PALLIATIVE CARE TEAM

Guidelines suggest that professionals with skills to meet the patient’s and family’s physical, psychological, social, and spiritual needs participate in the creation of a specialized care plan. Ideally, teams are interprofessional and include a nurse, physician, social worker, and chaplain, as well as other professionals, depending on the need.²¹ Many professional disciplines have developed specialized certification or training in palliative care (Box 52.1).

Where Is Palliative Care Delivered?

In the United States, palliative care is often delivered by a consult service in hospitals or in an inpatient unit.⁶ Approximately two thirds of U.S. hospitals and 85% of middle-to-large hospitals have palliative teams, but again, access varies, depending on the geography and type of hospital.²² The south-central states have the least access to palliative care with less than one third of hospitals in Arkansas, Mississippi, and Alabama reporting a palliative care team. By contrast, the northeast has the best access to palliative care. All hospitals in New Hampshire and Vermont report palliative care programs, as do 89% in Rhode Island and 88% in Massachusetts. While cancer patients who are admitted to the hospital may have high mortality and often have symptoms that are difficult to manage, only 20% to 26% of U.S. cancer centers offer dedicated palliative care inpatient beds.^{6,23} Palliative care clinics are increasingly available, but home palliative care for patients who are not eligible for hospice is rare in the United States due to lack of reimbursement.⁶

INPATIENT PALLIATIVE CARE TEAMS

Outcomes With Palliative Care Teams

Inpatient palliative care teams reduce hospital costs and resource utilization. A retrospective study of six hospitals with well-established palliative care teams showed a decrease of \$1700 per admission for patients discharged alive and \$5000 for patients who died.^{23a} A study of Medicaid beneficiaries showed hospital costs decreased by an average of \$6900 during an admission once palliative care teams became involved with reduced intensive care unit (ICU) length of stay²⁴ and fewer ICU deaths.²⁵ A cohort study of over 41,000 inpatients who received an inpatient palliative care consultation for goals of care showed significantly reduced future acute care costs, healthcare utilization, and 30-day readmissions when compared with a propensity-matched cohort that did not receive a palliative care consultation.^{25a} Studies examining inpatients with advanced cancer have demonstrated greater cost savings when a palliative care consultation is requested earlier in the hospital stay,^{25b}

BOX 52.1 Members and Roles in a Palliative Care Team

Physician	Diagnoses, treats, and manages a wide variety of medical issues for patients Provides expert symptom management and consultation Provides expert skills and consultation in communication with patients who are seriously ill, their families, and other providers
Nurse	Participates in the diagnosis, treatment, and management of acute and chronic serious illnesses within his or her scope of practice Assesses the patient’s psychosocial and spiritual needs in the setting of a serious illness Participates in symptom management within his or her scope of practice Uses unique skillsets to communicate with the patient, family, healthcare team, and community
Social worker	Addresses the psychosocial needs of patients and their families affected by serious illness Participates in meetings with the medical team, patients, and families Assists in complex discharge needs and communicates with community resources
Spiritual advocate	Assists patients and families in identifying and addressing spiritual distress related to serious illness Provides or facilitates appropriate spiritual or religious rituals Provides liaison services to community spiritual resources
Additional professionals who provide expertise to the palliative care team	Anesthesia pain experts Pharmacists Rehabilitation therapists Psychiatrists

Note: Roles and competencies may vary by region and training. Data from the following resources: National Association of Social Workers. The certified hospice and palliative social worker. <https://www.socialworkers.org/Careers/Credentials-Certifications/Apply-for-NASW-Social-Work-Credentials/Certified-Hospice-and-Palliative-Social-Worker>. Accessed March 19, 2019; Hospice and Palliative Nurses Association. <http://www.hpna.org/DisplayPage.aspx?Title=Position Statements>. Accessed June 20, 2013. Board of chaplaincy certification. Palliative care specialty certification competencies. <http://bcci.professionalchaplains.org/content.asp?admin=Y&pl=45&sl=42&contentid=49>. Accessed June 20, 2013. Center to Advance Palliative Care. <http://www.capc.org>. Accessed June 20, 2013.

and in patients with more comorbidities.^{25b} Earlier palliative care consultations also help to facilitate building consensus around goals of care and use of invasive means to support life.²⁶ Inpatient palliative care teams improve patient-centered outcomes including quality of life,²⁷ patient and caregiver satisfaction,²⁷ and, to a variable degree, symptoms.^{28,29} Importantly, palliative care consultation does not increase in-hospital mortality,^{24,30} and even has been shown to lead to fewer days in the hospital and fewer inpatient deaths.^{30a} This fact may be

important for families and patients who incorrectly view palliative care as hastening death.

When to Consult Palliative Care Teams

Basic palliative care knowledge and skills are necessary for all clinicians; however, certain situations call for the expertise of a palliative care specialist. A variety of indicators have been developed to help physicians decide when a specialty palliative care assessment should be performed. Patients' palliative care needs should be assessed first by the treating physician, then a consultation with a palliative medicine specialist should follow when warranted. The presence of a potentially life-limiting (e.g., multiorgan failure, major trauma, sepsis) or life-threatening condition (e.g., metastatic cancer, cirrhosis, chronic renal failure) serves as the foundation for specialty palliative care involvement.³¹ The palliative care candidate should also fit at least one additional criterion, such as frequent hospital admissions for the same condition, functional decline, or an ICU stay of 7 days or longer. More specific consultation criteria should take into account the local hospital system, resources, and patient population. Each hospital should develop a procedure for identifying patients who would benefit from palliative care consultation,³¹ which often includes assistance with symptoms that are difficult to control, complex decision making, and provider or family support.

Palliative Care in the Surgical Intensive Care Unit

The three main models of palliative care integration in the ICU are the consultative model, the integrative model, or a hybrid model.³² In the consultative model, a specialist palliative care team makes recommendations to the primary physician regarding the care of the patient. In the integrative model, the surgeon or intensivist identifies and addresses issues related to palliative care without specialist input. Hybrid models that combine the two approaches above also exist. The most effective model is not clear at this point and is often determined by hospital resources and culture.

Many quality improvement efforts have been proposed to improve palliative care integration into ICUs.^{32a} One such effort involved screening of critically ill patients followed by direct communication between palliative care providers and intensivists for patients meeting prespecified criteria. This led to increased palliative care consultations in the medical intensive care unit (MICU) by 113% and in the surgical intensive care unit (SICU) by 51% over a 1-year timeframe.^{32b} Although initial palliative care efforts and research have focused on MICUs, increased attention is being focused on providing palliative care to appropriate patients in the SICU.³²

Trigger Criteria in the Surgical Intensive Care Unit

Surgical patients who die in the ICU often follow one of two courses. The first is characterized by a prolonged hospital stay with multiple transitions between acute care and ICU settings and intervening periods of prognostic uncertainty, while the second often occurs in trauma patients or other more acutely ill surgical patients with a rapidly declining course.³² One study of patients in a trauma ICU showed that early assessment of patient and family preferences and early interdisciplinary meetings led to unchanged mortality, do

not resuscitate (DNR) orders, and withdrawal of life support; however, the DNR and withdrawal orders were completed earlier in the hospital stay, and the ICU length of stay decreased in patients who ultimately died.²⁶ Focus on identification of appropriate palliative care consultations early in the hospital course is increasingly important, particularly in the former group.

Use of trigger criteria, in which the presence of one or more predefined patient risk factors results in automatic palliative care consultations, has shown encouraging results.²⁴ In a broad population of critically ill patients, the use of specific screening criteria to proactively initiate a palliative care referral decreases ICU resources utilization without affecting mortality.^{32c} Employment of these screening or trigger criteria encourages proactive and systematic patient screening, thereby eliminating the biases of individual providers in identifying patients that would benefit from palliative care team involvement.³² For example, one study examined the effect of implementing a structured palliative care intervention followed by an interdisciplinary family meeting within 72 hours of admission for all liver transplant service patients admitted to the SICU.^{32d} After the intervention, increases were seen in goals of care discussions on rounds, documented patient code status, and withdrawal of life support, whereas decreases were seen in time to placing a DNR order and ICU length of stay. There was no difference in mortality, and family members indicated that they had more time with their loved one.^{32d}

The most effective trigger criteria for palliative care consultations in SICUs have not been defined.³² Creation of universal criteria is complicated by variation among surgical patient populations, along with many other factors. Many proposals include some combination of these considerations: lengths of stay in the ICU, the lack of improvement during the ICU stay, the patient's age, and the patient's illness.³² One study performed in the SICU used 10 triggers based on expert opinion. These triggers included multiorgan system failure, SICU stay longer than 1 month, more than three SICU admissions during one hospitalization, and death expected during a current SICU admission.³³ This study showed no increase in palliative care consultation, but only 6% of the patients in this study met the trigger criteria, and although the attending physician was notified when a patient met the criteria, palliative care consultation was still left to the judgment of the attending physician.³³ A more inclusive screening process or a mandated palliative care referral, as observed in some of the successful medical ICU studies,²⁴ may have altered these results. Current recommendations suggest that referral criteria should be informed by available data but individualized for each hospital, or even each ICU, using input from stakeholders including palliative care providers, intensivists, hospital leadership, and nonphysician ICU care providers.^{32c}

OUTPATIENT PALLIATIVE CARE

Outpatient palliative care clinics exist to follow patients after discharge or to provide outpatient symptom management and psychosocial support.³⁴ The providers, availability, and focus vary widely.³⁴ A landmark study by Temel in 2010 randomized 151 patients with metastatic

non-small-cell lung cancer to early outpatient palliative care plus the standard oncologic care or standard oncologic care alone. Patients in the palliative care group had higher quality of life scores, as well as fewer symptoms of depression.³⁵ Perhaps most surprisingly to some, the patients in the palliative care group lived a median of 2.7 months longer than those in the standard care group, despite receiving less aggressive care.³⁵ These results and others have led to a recommendation by the American College of Chest Physicians that palliative care be introduced early in the course of disease for patients with stage IV lung cancer or a high symptom burden.³⁶ A systematic review of patients with a variety of terminal illnesses showed that outpatient palliative care improved depression and quality of life, reduced aggressive care at the end of life, increased advanced directives, reduced hospital length of stay and hospitalizations, and improved family and caregiver satisfaction. A Cochrane review found that while the effect sizes were small, early palliative care interventions may improve quality of life and symptom intensity in patients with advanced cancer. In 2017, because of multiple new randomized controlled studies in other cancers, the American Society of Clinical Oncology Clinical Practice Guideline expanded their recommendations for early palliative care consultation to cover all advanced cancer, not just advanced lung cancer.

Differences Between Hospice Care and Palliative Care

In contrast to palliative care, the definition of hospice care as it applies to the type of patient, the involvement of the medical team, and the setting, varies between countries.³⁹ In some countries, the terms hospice care and palliative care are interchangeably used, but in the United States, hospice care refers to a benefit provided by the governmental healthcare system. Patients are eligible to enroll in hospice care when their life expectancy is less than 6 months, and typically after life-prolonging treatments, such as chemotherapy, are stopped. Despite the logistic differences, the philosophy of hospice care generally focuses on reducing suffering, enhancing the quality of life, and supporting the patient and family (Fig. 52.4).

HOSPICE CARE IN THE UNITED STATES

In the United States, hospice is a per-diem capitated payment system for a defined set of services for patients with a life expectancy of 6 months or less, as agreed on by two physicians.⁴⁰ Medicare pays for approximately 80% of hospice care in the United States, and many private insurers have established similar guidelines. These services include visits to a patient's residence by a nurse (the main provider of clinical care⁴¹), aide, social worker, and chaplain.⁴⁰ Family members are also eligible to receive a year of bereavement counseling.⁴⁰ Continuous care and short-term hospital admission are available for patients with uncontrolled symptoms. A core set of requirements for the hospice benefit exists (Fig. 52.5). However, beyond these requirements, each hospice unit can decide which treatments to cover, and this coverage can vary widely. For example,

Continuous Features	
• Multidisciplinary team	• Focus on quality-oriented care
• Symptom management: pain, dyspnea, psychosocial	
• Family support	
• Attempts to minimize suffering	
Early Palliative Care	
• Appropriate at any stage of serious illness	• Hospice Care
• Often provided in hospitals or outpatient clinics	• Prognosis <6 months (can be renewed every 60 days)
• Can be used in conjunction with "aggressive" care	• Focus on home-based care
• Free-for-service model	• Patient usually agrees to focus on comfort rather than life-prolonging treatments
	• Through Medicare, billed on a per-diem rate

Fig. 52.4 Features of palliative care and hospice care in the United States.

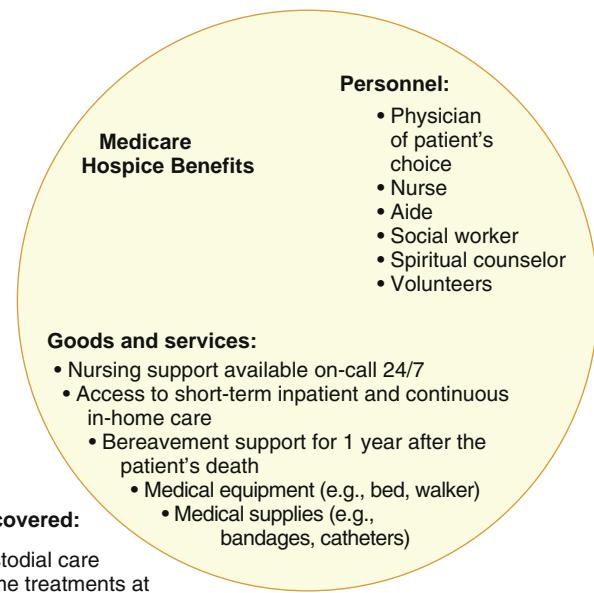


Fig. 52.5 Aspects of the Medicare hospice benefits.

some hospice organizations may cover palliative radiation treatments, whereas others may not. Patients who outlive their 6-month prognoses may have their benefits extended in 60-day increments after a face-to-face visit with a physician, recertifying that the patient continues to meet hospice criteria.

Who Is Eligible for Hospice Care?

To qualify for hospice, an attending physician and a hospice medical director must certify that the patient's prognosis is less than 6 months if the disease runs its normal course.⁴⁰ Medicare has created guidelines that describe eligibility criteria for hospice services, although the opportunity for interpretation does exist. For example, the criteria for a patient with chronic lung disease include disabling dyspnea at rest, poor response to bronchodilators, hypoxemia at rest, and repeated hospitalizations for emergency department visits.⁴¹ As a result of the subjectivity of some of the

guidelines, some hospices may accept patients that other hospices deem ineligible. Patients are not required to have a DNR order to be enrolled in hospice.

Recipients of Hospice Care

Although patients with cancer were previously the primary recipients of hospice care, the proportion of patients receiving hospice care with noncancerous diagnoses such as dementia, chronic obstructive pulmonary disease (COPD), and congestive heart failure (CHF) has increased from 16% in 1990 to 69% in 2010.⁴² This increase is particularly problematic, considering the lack of good prognostic criteria for a 6-month life expectancy in some disorders, which can complicate hospice referral timing.⁴³ During this same period, the percentage of patients with Medicare who died while receiving hospice care increased from 5.5% to 44%,⁴² yet the length of enrollment in hospice remains abbreviated. The median length of stay in hospice was 18 days in 2010,⁴² and approximately one third of all hospice patients lived for less than 1 week after admission to hospice care.⁴¹ Based on utilization review, 14.3% of Medicare patients with cancer did not enroll until the last 3 days of life.^{43a} This trend toward late admission suggests that many patients are referred to hospice well after they are eligible.

Outcomes of Hospice Care

Hospice care decreases patient symptom burden⁴⁴ and increases caregiver satisfaction, with 98% of family members recommending hospice care to others.⁴¹ A survey of over 1500 bereaved family members showed that 70% of respondents whose family member received hospice services considered the care “excellent” with less than 50% of those with decedents receiving home health services considering the care “excellent.”⁴⁵ Studies related to cost effectiveness vary in their conclusions. Yet, a few studies suggest that the length of hospice use is correlated with cost savings.^{44,46} A 2007 study by Taylor suggested cost savings with a hospice stay of 53 to 107 days,⁴⁶ whereas a 2013 study by Kelley showed cost savings with shorter hospice stays as well.⁴⁴ In a study looking at projected savings for beneficiaries with poor-prognosis cancers, increasing hospice utilization from 60% to 80% and increasing duration from 2 to 6 weeks could save \$1.79 billion annually.^{46a}

PALLIATIVE CARE AND ANESTHESIOLOGISTS

Anesthesiologists, as well as subspecialists in pain management and critical care medicine, are likely to interact with patients who are receiving palliative care services. Awareness of the goals of care in the palliative and hospice setting and what services are provided will help the anesthesiologist develop an appropriate plan based on the individual patient’s goals. Critical care anesthesiologists are often called upon to aid in the determination of hospice eligibility and to help families discuss care plans. Pain medicine physicians may provide medication management and interventional procedures alongside palliative care physicians or as part of hospice benefit.

Surgery in Seriously Ill Patients

Palliative surgery has been defined as “the deliberate use of a procedure in a patient with an incurable disease

with the intention of relieving symptoms, minimizing patient distress, and improving the quality of life.”⁵¹ A 2004 study of over 1000 patients with advanced cancer undergoing palliative surgery showed a 30-day morbidity of 29% and mortality of 11%, with 80% of patients experiencing improved symptoms at 30 days. A similar study by the same author in 2011 showed a significant improvement from their earlier study. Of 227 patients, there was a morbidity of 20% and mortality of 4%, with 90% experiencing symptom resolution.^{51,53} The study authors attribute some of this change to better patient selection through shared decision making with patients and families.⁵¹

Communicating Surgery Risk in Seriously Ill Patients

Decision making concerning surgery near the end of life is complex; while some surgeries may increase quality of life or allow a patient to achieve a specific goal, others may result in excessive pain, functional decline, prolonged ICU or hospital stay, or increased use of resources without a clear benefit. A need exists to improve the quality of preoperative communication, to support decision making by surgeons and patients, and to prioritize advance care planning for patients undergoing high-risk surgery. Despite the recognized risk of performing surgery in high-risk patient populations, many patients do not have a complete understanding of the wide range of possible outcomes associated with surgery.^{53a} The mental frameworks often employed by surgeons and their patients can contribute to both a lack of understanding of possible outcomes and the formation of a contractual obligation to engage in maximal life-sustaining measures after surgery.^{53b-d} Both of these issues may result in provision of care that is not well-aligned with patient goals and preferences.

Communication frameworks exist that can assist in conducting preoperative conversations with patients considering high-risk surgery.^{53e,f} The “Best Case/Worst Case” tool uses a shared decision-making model with a visual aid to explain the best case scenario, the worst case scenario, and the most likely outcomes related to both surgery and conservative management (Fig. 52.6).^{53f} This tool allows the surgeon to elicit treatment preferences that are informed by realistic outcomes. Optimal use of the Best Case/Worst Case tool takes patient-specific comorbidities and risk factors combined with surgery-specific risk into account when explaining possible outcomes to patients considering high-risk surgery. A qualitative analysis of the Best Case/Worst Case tool using focus groups of both surgeons and older patients who had been involved in making a medical decision for themselves or their family members within the last year was conducted.^{53f} From a patient perspective, the tool was seen as favorable overall in that it establishes a choice, allows visualization of distinct paths to help in decision making, and encourages deliberation based on a variety of treatment preferences. Surgeons pointed out that use of this tool provides a useful structure to guide the conversation, allows discussion of patient preferences, and may legitimize non-operative treatment options as still providing care rather than doing nothing. Use of tools such as this one may improve a patient’s understanding of potential complications and consequences of choosing a

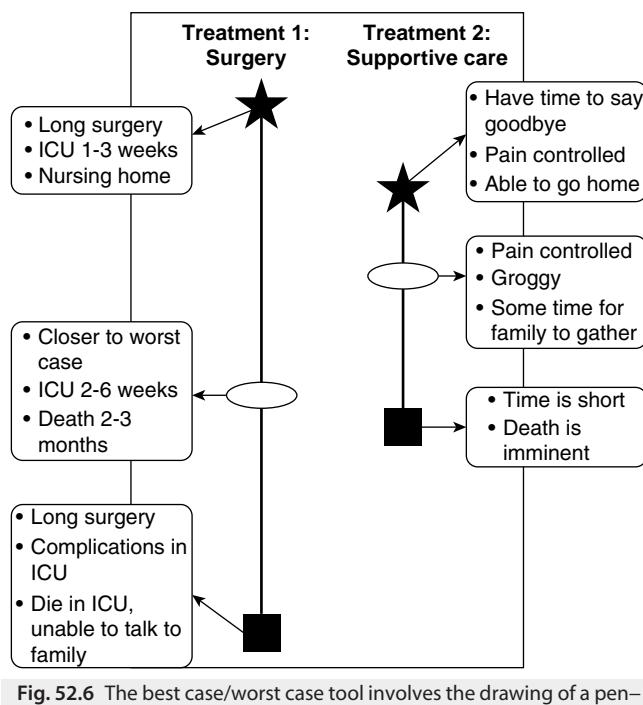


Fig. 52.6 The best case/worst case tool involves the drawing of a pen-and-paper diagram by the physician. A vertical bar depicts each treatment option, and the length of the bar represents the range of possible outcomes. A star represents the best case, a box the worst case, and an oval the most-likely outcome. The physician describes each “case” using narrative derived from clinical experience and relevant evidence and writes key points on the diagram. *ICU*, Intensive care unit. (Redrawn from Kruser J, Nabozny MJ, Steffens NM, et al. “Best case/worst case”: Qualitative evaluation of a novel communication tool for difficult in-the-moment surgical decisions. *J Am Geriatr Soc*. 2015;63[9]:1805–1811.)

specific therapy, which allows them to elect the treatment option that is best aligned with his or her goals near the end of life.

Anesthetic Concerns in the Patient Receiving Palliative Care

PREOPERATIVE CONSIDERATIONS

A patient’s decision-making capacity may change during a hospitalization or over time and should be assessed before seeking consent from the patient for anesthesia. As noted in [Chapter 8](#), when a standing DNR order exists in a patient awaiting surgery, a discussion of the patient’s goals and the creation of a plan for intraoperative and postoperative management that meets the patient’s goals should occur prior to surgery. In the case of the perioperative reversal of a DNR order, a plan for when to reinstitute that order should be developed [53g](#) and discussed with the surgeon and nurse as appropriate.

A thorough preoperative evaluation of the patient’s disease should also take place with attention to the patient’s cognitive status, recent medications (including chemotherapy), presence of metastases, and wounds. Knowledge of the patient’s preoperative functional status and prognosis may impact the anesthetic plan and also may inform an accurate assessment of risks and benefits. Details on special considerations in specific disease states such as cancer,

COPD, and others are included in [Chapter 32](#). Considering the number of patients receiving palliative care who may be on large doses of opioids perioperatively, anesthesiologists are advised to follow the guidelines in [Chapter 51](#) regarding perioperative pain management.

INTRAOPERATIVE CONCERNS

Resuscitation status should be communicated to any perioperative providers caring for the patient. Consideration should be given to postoperative nausea and vomiting prophylaxis, and the care of fragile skin in this population. Patients may have coagulopathies, thrombocytopenias, or neutropenias that may preclude them from receiving regional or neuraxial anesthesia, thereby impacting their intraoperative pain management.

ANESTHETIC CHOICE AND CANCER

Recent studies have attempted to clarify the role of anesthesia in cancer progression and recurrence. Studies of the effect of regional anesthesia on those with cancer are mixed but suggest a possible mortality benefit, [53h](#) although meta-analyses have not found either a beneficial nor detrimental effect of regional versus general anesthesia regarding cancer recurrence. [53i](#) Additional discussion is available in [Chapter 45](#). Studies that examine the choice of specific systemic anesthetics on cancer are mostly *in vivo* or *in vitro*, but available data also suggest differences in responses to tumor cells among the different drugs ([Table 52.1](#)). [53j](#)

POSTOPERATIVE COURSE

Standard postoperative care is adequate for most patients in palliative care. Risks for postoperative pain, delirium, and nausea and vomiting may be increased, depending on the individual patient. Providers should communicate any limitations in care and when limitations revert to their preoperative status.

Communication

Communication about goals of care and treatment preferences influence many outcomes in patients with serious illness. Better communication has been associated with improvement in quality of life, decreased use of life-prolonging therapies near the end of life, provision of care that is more consistent with patient preferences, and earlier hospice referrals. [53k](#) The American College of Physicians describes communication with seriously ill patients as a “low-cost, high-value intervention.” [53k](#) The American College of Physicians recommends that communication be initiated early in the course of life-threatening illness, and ideally by a physician with an established relationship with the patient. [53k](#)

ADVANCE CARE PLANNING

The Patient Self-Determination Act, which took effect in the United States in 1991, requires healthcare providers and institutions to advise patients of their right to an

TABLE 52.1 Anesthetic Drugs and Host Defenses

DRUG	POTENTIAL EFFECT ON ANTITUMOR HOST DEFENSES
Ketamine	Reduces natural killer (NK) cell activity and the number in animal models
Thiopental	Reduces NK cell activity and the number in animal models
Propofol	Reduces NK cell number in animal models
Volatile agents	Inhibits interferon stimulation of NK cell cytotoxicity in animal models Reduces NK cell number in humans; is associated with worse outcomes when compared with local anesthesia for melanoma excision
Nitrous oxide	Associated with acceleration in the development of lung and liver metastases in animal models No effect on cancer outcomes after surgery for colorectal carcinoma in humans Inhibits the formation of hematopoietic cells that may be important for tumor cells
Local anesthetic drugs	Lidocaine inhibits epidermal growth factor (EGF) receptor and tumor cell proliferation <i>in vitro</i> ; ropivacaine inhibits growth of cancer cells
Morphine	Inhibits cellular immunity including NK cell activity in animal models Inhibits NK cell activity in humans
Fentanyl	Inhibits NK cell activity in humans
Tramadol	Stimulates NK cell activity in animal models Stimulates NK cell activity in humans
Cyclooxygenase-2 (COX-2) inhibitors	Display anti-angiogenesis and antitumor effects in animal models

From Snyder GL, Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. *Br J Anaesth.* 2010;105:106–115.

advance directive and to develop institutional policies and education regarding advance directives.⁵⁴ However, since the introduction of advance directives, multiple issues have been identified, such as amending preferences as the illness and circumstances change.^{55–57} Understanding a patient's goals requires open communication with the patient and physician and sometimes repeated conversations to clarify and update the goals of treatment as the patient's condition changes. More information on advance directives and decision-making surrogates can be found in [Chapter 8](#).

OUTCOMES OF ADVANCE CARE PLANNING

The landmark 1995 Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) was a 2-year prospective observational study, followed by a 2-year randomized trial of 9105 patients in five U.S. teaching hospitals, with the goal of improving end-of-life decision making.¹⁴ The study enrolled patients with advanced stages of nine illnesses and a 6-month mortality

of 45% to 48%. The observation period showed that 49% of patients who did not want cardiopulmonary resuscitation (CPR) did not have a written DNR order, and that the physicians were often unaware of the patients' wishes.¹⁴ In the intervention, prognostic data were made available to physicians, and a nurse was available to facilitate information sharing, advance care planning, and pain assessment. This intervention did not have any negative impact on physician communication, pain, use of hospital resources, or other measured outcomes.²¹ Although more advance directives were documented, only 14% of the patients spoke with a physician when completing their advance directive, and only 25% of the physicians were aware of their patients' advance directives a week after hospital admission.⁶¹ Similar studies did not demonstrate that advance directives influenced the types of care or the resources used.^{62,63} These studies suggest that efforts toward increasing advance directives alone are insufficient to drive any changes in care.

Many barriers exist to advance care planning, including timing, setting, and quality of communication. Even though physicians often perceive successful communication about treatment planning with patients, data suggest that patient perceptions of treatment options and prognosis often vary considerably.^{63a} For example, between 50% and 75% of patients with incurable cancer perceived that chemotherapy, radiation therapy, or surgery could lead to survival.^{63a} It is not clear whether this discordance results from failure in physician communication, inability of the patient to understand and accept the information presented, or a combination of the two. Many professional organizations suggest that end-of-life care planning should begin in the outpatient setting when the patient has approximately 1 year to live.^{63a} However, in reality, these discussions often do not occur until much later in the patient's course, such as when an invasive intervention such as mechanical ventilation is needed.^{63b}

A variety of factors prevent use of advance directives around the time of high-risk surgery,^{63c–e} including surgeon perception.^{53d} Over half of the surgeons in a national survey indicated that they would not operate on a patient who expressed a desire to limit life-sustaining interventions postoperatively.^{63d} However, patients who have previously undergone high-risk surgery have indicated retrospectively that a greater preoperative emphasis on three critical points would have been helpful: (1) the need for surgery versus alternative treatment options, (2) expectations for postoperative recovery, and (3) use of perioperative advance directives.^{53a} This study highlights the need for communication with patients and their families around the surgical management and represents an opportunity for anesthesiologists to play a role in facilitating these conversations.

PHYSICIAN COMMUNICATION SKILLS TRAINING

The physician's approach to communication about difficult issues can affect how patients and families perceive illness, death, and treatment options. These skills are being taught as part of medical school curriculum with increasing frequency, but retention of skills tends to be low.^{63f} Most physicians are less comfortable discussing code status than they

are with other topics, such as consent for procedures.⁶⁴ Between 40% and 75% of physicians, depending on their level of training, assess their own knowledge of delivering “bad news” as inadequate.⁶⁵ Despite the fact that the American Board of Surgery includes basic knowledge and skills in palliative care as a requirement for board certification in surgery,^{65a} only 9% of surveyed surgical residents believed they “received adequate training in palliation” during residency.⁶⁶ Similarly, as many as 90% of internal medicine residents expressed a desire for additional training in discussing topics such as DNR orders.⁶⁷ Despite this lack of training, residents often are the ones to talk about these issues with patients,⁶⁸ highlighting the importance of education in this area.

PHYSICIAN COMMUNICATION SKILLS

Physicians often rate their communication skills favorably, but surveys of other practitioners and of patients suggest that physicians may not be able to self-assess accurately. One study in an ICU showed that 90% of surgeons were satisfied with their communication skill concerning prognosis, but only 23% of intensivists and 3% of nurses rated the same skill favorably.⁶⁹ Similarly, patients’ perceptions of their cancer stage and prognosis were often incorrect in one study, although oncologists thought they were clear in their explanations of the illness.⁷⁰ Recordings of physician discussions with patients and families show that physicians focus on technical detail, avoid emotional topics, and tend to dominate the conversations,⁷¹ despite increased family satisfaction when the family spoke more and physicians exhibited more supportive behaviors.⁷¹ Even when a conversation takes place between a physician and a patient, the physician and patient may not agree on the outcome. One study of patients with metastatic cancer showed that physicians misunderstood their patients’ preferences for CPR 30% of the time.⁷² Currently, no comparable studies regarding anesthesiologists have been conducted. These findings highlight the importance of assessing a patient’s understanding of his or her disease process before a procedure is performed or during an ICU stay.

The Surgical “Contract”

When caring for surgical patients, it is important to understand the conceptual frameworks that frequently influence both providers and patients in their approach to care. First, many patients perceive that surgery will “fix” their acute abnormality and restore normalcy to their lives,^{53f} rather than potentially contribute to further functional or cognitive decline. The potential for the latter problems is rarely discussed preoperatively. In addition, the relationships between surgeons and their patients are unique from other relationships in medicine, because many surgeons perceive an implicit “contractual” agreement to pursue maximal life-sustaining measures after surgery.^{53c,d,72a} Surgeons are said to subscribe to a covenantal ethic, meaning that the surgeon takes on individual responsibility for the patient’s life once he or she performs surgery.^{72a} An ethnographic study examining differences in end-of-life management of surgical patients in three ICUs—one unit run by trauma surgeons, one unit co-managed by

surgeons and intensivists, and one unit run by intensivists—identified divergent priorities between surgeons and intensivists. While many intensivists considered use of scarce resources more globally in their decision making, surgeons tended to focus on the individual patient only and delay withdrawal of life-sustaining treatment even when it was requested by family.^{72a} Surgeons and intensivists often also delivered differing messages regarding treatment and prognosis.^{72a} A study evaluating recorded preoperative conversations conducted by surgeons performing high-risk surgery found that surgeons often described high-risk surgery as “big surgery” and focused on the technical aspects of surgery during their preoperative conversations.^{53b} If they discussed need for life support after surgery, they focused on standard recovery rather than potential longer-term complications (e.g., prolonged mechanical ventilation or dialysis). Furthermore, while many surgeons perceived that a contractual agreement to pursue aggressive postoperative care had been made, only rarely did they make this contract explicit with their patients.^{53b} Other communication breakdowns may occur at the level of the patient (i.e., anxiety, fear, or inability to understand) or the medical system (i.e., time constraints, lack of advance care planning) and also contribute to decisions to proceed with nonbeneficial surgery.^{53e} Having a good understanding of these unique communication challenges in surgical patients at the end of life may help to facilitate communication with patients, families, and the care team.

WHAT DO FAMILIES CONSIDER IMPORTANT IN END-OF-LIFE COMMUNICATION?

A majority of family members consider trust in the treating physician and truthful communication about the patient’s illness as two of the most important factors in receiving quality end-of-life care.⁷³ Families have greater satisfaction when a higher level of decision making is shared.⁷⁴ In family meetings, family satisfaction increases with the number of empathetic statements made by a physician during a meeting.⁷⁵ Virdun and associates conducted a meta-synthesis of 16 qualitative studies examining factors that patients and families describe as important during inpatient end-of-life care.^{75a} Within the theme of effective communication and shared decision making, family members identified honest and clear communication using simple, understandable language; provision of information necessary to help make decisions; and engaging both the patient and family members in care planning as priorities.^{75a}

A variety of patient and family preferences influence the quantity of information desired and how to receive it. These preferences may be informed by a combination of personal, cultural, and family characteristics; however, physicians should not assume a preference based on a patient’s race or ethnicity.⁷⁶ Many practitioners use a question such as, “How much would you like to know?”,⁷⁷ although no studies of patient perceptions of that approach have been conducted. One study of patients with cancer indicated that some patients’ preferences for involvement in decision making changed over the course of the illness.⁷⁸ A few studies have noted that caregivers wanted more information than

the patients.⁷⁹ Some patients may indicate that they do not want to know about their condition and name a surrogate decision maker instead.

SPIRITUALITY AT THE END OF LIFE

Spirituality refers to the ways in which a person expresses meaning or purpose and affects an individual's sense of connectedness to the world around them. Religion may be a component of spirituality for some people, but many other aspects of spirituality also exist. Swinton and colleagues conducted a qualitative study where patients, family members, and clinicians involved in the care of 70 patients dying in the ICU underwent semistructured interviews.^{79a} Respondents perceived dying as a spiritual process. They reflected that spirituality comprises an important part of a patient's narrative before, during, and after death. Serious illness and the prospect of death can bring a number of spiritual issues to the foreground for patients and families, from questioning the meaning of one's life to a religion's teaching on specific medical interventions.⁸⁰ Patients typically want physicians to ask about their spiritual preferences⁸¹ and describe their spiritual needs as frequently remaining unmet.⁸² A simple screening question such as, "Is religion or spirituality important in your life?" has been proposed and may help identify patients in whom a spiritual need exists. Asking about religion and spirituality may provide a context for the healthcare team, since many patients and families make decisions based on these beliefs.⁸³ Physician understanding of the reasoning behind their patients' decisions is likely to improve end-of-life care.

COMMUNICATION FRAMEWORKS

The prior studies, which demonstrate frequent misunderstandings and poor communication, emphasize the need for an understanding of the importance of effective communication among all participants.⁸⁵ A number of frameworks have been developed to aid physicians in discussions with patients and families.⁸⁶⁻⁸⁸ No study has compared their relative effectiveness on patient or family outcomes, and very few assessed the effect of a specific communication framework on outcomes.⁷⁷ Commonalities in the approaches include active listening, validating patient concerns, and assessing understanding. A recommended comprehensive conversation guide developed by synthesizing data collected in multiple qualitative studies includes the following elements: set up the conversation, assess understanding and preferences, share prognosis, explore key topics (i.e., goals, fears and worries, sources of strength, critical abilities, tradeoffs, and family), close the conversation, document your conversation, and communicate with key clinicians (Fig. 52.7).^{88a}

Family Meetings

Family conferences in the ICU have increasingly been used to facilitate information sharing between families and providers. In the ICU setting, meetings held within 72 hours of admission have shown decreased lengths of stay without increased mortality.⁸⁹ One of the few studies that evaluated a standardized communication approach was a single-site

study of families of patients who were seriously ill and randomized to either a standardized communication template with a bereavement brochure or the standard care.⁸⁷ The communication intervention structured around the mnemonic of VALUE (value, acknowledge, listen, understand, elicit questions) emphasizes empathy, understanding of the patient as a person, and allowing family members to ask questions.⁸⁷ Family members in the study arm had decreased symptoms of psychological distress in a survey 3 months later (Box 52.2).⁸⁷

Many physicians struggle with how to begin family meetings. Common approaches include: introducing the family and team members, eliciting the level of understanding from family members, and briefly summarizing the purpose of the meeting; for example, "What have you been told about what's going on with your dad?".

Breaking Bad News

The six-step SPIKES (setting, perception, invitation, knowledge, empathy, sequelae) protocol is a framework for breaking bad news. Several of the elements, such as finding a quiet meeting space, asking what the patient or family understands, and making a plan for the future, apply in many situations (Box 52.3).⁸⁶ A meta-synthesis of available qualitative data suggested that breaking bad news is a skill that requires the provider to reassess and adapt the conversation based on a number of factors including the provider-patient relationship, responses from the patient and family, the environment, and cultural or social factors.^{89a}

Responding to Emotion

The NURSE (name, understand, respect, support, explore) protocol is a framework for responding to emotion, including anger. Patient and family anger directed toward healthcare providers is common in the setting of serious illness.⁹⁰ Crucial concepts in responding to anger include not becoming defensive or personalizing the anger, respectfully listening, and setting appropriate boundaries for safety.⁹⁰ Although difficult to accomplish in the moment, viewing anger as a coping mechanism in the grieving process is often helpful (Box 52.4).⁹¹

Requests for Nondisclosure

Family members may ask physicians to withhold a diagnosis from the patient. The cultural norms for disclosing a patient's diagnosis vary widely among cultures and countries. In the United States, the culture of disclosure has rapidly changed, and now most physicians expect to disclose the prognosis to the patient.⁹² No evidence is available that recommends how to deal with requests for nondisclosure, but expert opinions recommend empathetically responding to the family member, trying to understand the family's concerns about disclosing the prognosis, and asking the patient how and if he wants to be involved. For example, "Some people want to be told about any health issues and make their own decisions, while others prefer for a family member to be told the medical information and to make the decisions. What would you like?"⁹³

Time-Limited Trials

In cases where the benefit of a clinical intervention is unclear for a specific patient, a time-limited trial, in which

Serious Illness Conversation Guide

PATIENT-TESTED LANGUAGE

SET UP

"I'd like to talk about what is ahead with your illness and do some thinking in advance about what is important to you so that I can make sure we provide you with the care you want — **is this okay?**"

ASSESS

"What is **your understanding** now of where you are with your illness?"

"How much **information** about what is likely to be ahead with your illness would you like from me?"

SHARE

"I want to share with you **my understanding** of where things are with your illness ..."

Uncertain: "It can be difficult to predict what will happen with your illness. I **hope** you will continue to live well for a long time but I'm **worried** that you could get sick quickly, and I think it is important to prepare for that possibility."

OR

Time: "I **wish** we were not in this situation, but I am **worried** that time may be as short as __ (express as a range, e.g. days to weeks, weeks to months, months to a year)."

OR

Function: "I **hope** that this is not the case, but I'm **worried** that this may be as strong as you will feel, and things are likely to get more difficult."

EXPLORE

"What are your most important **goals** if your health situation worsens?"

"What are your biggest **fears and worries** about the future with your health?"

"What gives you **strength** as you think about the future with your illness?"

"What **abilities** are so critical to your life that you can't imagine living without them?"

"If you become sicker, **how much are you willing to go through** for the possibility of gaining more time?"

"How much does your **family** know about your priorities and wishes?"

CLOSE

"I've heard you say that __ is really important to you. Keeping that in mind, and what we know about your illness, I **recommend** that we __. This will help us make sure that your treatment plans reflect what's important to you."

"How does this plan seem to you?"

"I will do everything I can to help you through this."



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SI-CG 2017-04-18



Fig. 52.7 Serious illness conversation guide. (2015 to 2017 Ariadne Labs: A Joint Center for Health Systems Innovation [www.ariadnelabs.org] between Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health, in collaboration with Dana-Farber Cancer Institute. Licensed under the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License, <http://creativecommons.org/licenses/by-nc-sa/4.0/>.)

the physician and patient or family agree to reevaluate the benefit after a specified period, may be helpful.⁹⁴ Time-limited trials give families a sense of when the health-care team expects to know whether an intervention is helping and creates the expectation that the issue will be readdressed.

RESUSCITATION STATUS

Outcomes of Cardiopulmonary Resuscitation

CPR was introduced around 1960, initially as a treatment for intraoperative events⁹⁵ and then expanded outside the surgical unit. Outcomes of CPR have improved, with over

BOX 52.2 VALUE: Framework for End-of-Life Conferences

- Value:** Value and appreciate what the family member says. "Thank you for helping me understand how your husband's condition has changed over the past year."
- Acknowledge:** Acknowledge emotions. "This is often a sad time for families."
- Listen:** Actively listen. Remember to be silent and to give the family member time to speak.
- Understand:** Gain an understanding of the patient. Ask who the patient is as a person. "Can you tell me about your father, what kind of person he is and what's important to him?"
- Elicit questions:** Ask family members if they have questions. "We have discussed a lot of information. Do you have any questions?"

Data from Lautrette A, Darmon M, Megarbene B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med.* 2007;356:469–478.

BOX 52.3 SPIKES: Framework for Breaking Bad News

- Setting:** Arrange for a quiet, private space large enough for all participants.
- Perception:** Assess the participants' understanding. "What have the doctors told you about your wife's illness?"
- Invitation:** Ask how much information is desired. "Some people like all the details, others just like the big picture. What would you like?"
- Knowledge:** Tell the participants what is known, using language that is easy to understand and avoiding the use of complex medical phrases.
- Empathy:** Acknowledge emotions. "I wish things were different."
- Sequelae:** Agree on the next steps. "Let's meet tomorrow afternoon so I can update you on her condition."

Data from Baile WF, Buckman R, Lenzi R, et al. SPIKES—A six-step protocol for delivering bad news: application to the patient with cancer. *Oncologist.* 2000;5:302–311.

BOX 52.4 NURSE: Framework for Dealing with Emotion

- Name:** State the emotion you believe the patient or caregiver is exhibiting. "It seems like you are angry."
- Understand:** Empathize with and legitimize the emotion. "I can't imagine how hard this must be for you."
- Respect:** Praise the patient or caregiver for his or her strength. "You've done so much for your mother during this difficult time."
- Support:** Show support. "I want to help."
- Explore:** Ask the patient or caregiver to elaborate on the emotion. "Can you help me understand what was so frustrating today?"

Data from Back AL, Arnold RM, Baile WF, et al. Approaching difficult communication tasks in oncology. *CA Cancer J Clin.* 2005;55:164–177.

half the patients who suffer in-hospital cardiac arrest surviving the initial resuscitation and nearly one quarter surviving to discharge.⁹⁶ Survival is better for patients with a

shockable initial rhythm (37%) when compared with pulseless electrical activity (12%) or asystole (11%),^{96a} with time to defibrillation representing a critical factor in patient outcome.

Approximately 85% of cardiac arrests in surgical patients occur postoperatively, and this patient population may have a higher likelihood of survival than other groups of patients.^{97,98} In one large study of older surgical patients who survived to discharge after in-hospital CPR, approximately one half had moderate-to-severe neurologic defects⁹⁹ and 60% were alive 1 year later.⁹⁹ Induced mild hypothermia improves neurologic outcome after cardiac arrest, but benefits are better demonstrated in the out-of-hospital arrest population.^{99a} Data increasingly suggest that there are gender differences between outcomes after cardiac arrest. A study comparing outcomes in men and women after cardiac arrest showed that women who survived to discharge after cardiac arrest had worse cognitive, functional, and psychiatric outcomes after multivariate adjustment for multiple confounders.^{99b}

Resuscitation Status Discussions

Discussion of resuscitation status can be challenging to some providers.⁶⁴ Anesthesiologists may be involved in conducting discussions related to resuscitation status with patients in the ICU or in the perioperative period. Ideally, the discussion about code status takes place in the context of a conversation about the patient's overall health and goals. For example, one patient might decide on life prolongation as a goal, in which case a physician might recommend resuscitation attempts even if unlikely to succeed, whereas another patient with the same illness might prioritize physical independence as a goal, in which case the physician might recommend a DNR order to decrease the likelihood of prolonged ICU time or an unacceptable physical status. The impact of this approach is unknown. A small simulated study that played a standardized video of a code status discussion to cancer patients showed no difference between asking the patient his or her desired resuscitation status or making a suggestion for DNR order.¹⁰⁰ The few studies that formally examine the best way to approach discussions regarding resuscitation do not clearly demonstrate a single best approach.⁹⁵ For example, one study examined using the terminology "allow natural death" instead of "do not resuscitate" with terminal cancer patients and did not show that either term was favored over the other.^{100a}

Perioperative Limitations on Treatment

The American Society of Anesthesiologists has published guidelines related to orders for the limitation of treatment in the perioperative setting.¹⁰¹ The ethics of perioperative DNR orders are discussed more comprehensively in Chapter 8.

Prognosis

Multiple studies have examined the ability of physicians to prognosticate survival for a given patient. In a meta-analysis of eight studies in patients with a median survival

of 4 weeks, physicians overestimated the prognosis by approximately 30%.¹⁰⁸ Predictions were more accurate in patients with poorer performance status.¹⁰⁸ In a prospective cohort study of 365 physicians and 504 patients receiving hospice care, the physicians overestimated survival by a factor of 5, and 63% of their predictions were overestimates.¹⁰⁹ The longer a physician knew a patient, the more difficult it was for that physician to prognosticate.¹⁰⁹ Physicians in the ICU tend to be overly pessimistic. In a study of 851 patients receiving mechanical ventilation, only 71% of patients for whom a physician estimated a likelihood of survival of less than 10% at some point during their stay in the ICU died in the ICU.¹¹⁰ A meta-analysis suggested that physicians are more accurate at predicting mortality than algorithmic scoring systems (described in the “Prognostic Tools” section) in the first 24 hours after ICU admission; however, neither physicians nor scoring systems are reliably accurate for individual patients.¹¹¹ Overall, physician estimates do correlate with survival¹¹² and are more accurate in predicting mortality than other outcomes such as return to cognitive baseline.^{112a} For example, a study of 521 patients in a MICU found that physicians and nurses were unable to predict satisfaction with the quality of life 6 months after admission. In general, nurses tended to be more pessimistic than physicians and suggested withdrawal of life-sustaining treatment more often in patients who ultimately survived (Figs. 52.8 and 52.9).¹¹³ Prognostic tools that include clinician assessment are better than tools that rely on objective data alone, but the best predictions arise when multiple providers (physicians and/or nurses) agree on the prognosis.^{113a}

Difficulty with prognostication has led some physicians to avoid giving any kind of timeframe to eliminate the possibility of being wrong.^{114,115} However, 87% of 179 surrogate decision makers wanted the physician to give a prognosis, even if it was uncertain.¹¹⁶ Most understood the inherent unpredictability of prognostication and preferred that physicians make the prognostic uncertainty clear during the discussion.¹¹⁶ Prognosis, even in the face of uncertainty, can help families prepare for bereavement and make important decisions about coordinating work, visitors, and finances.¹¹⁶ Good data suggesting how to present prognoses to patients are not available. One approach to prognostication involves giving ranges such as hours to days, days to weeks, weeks to months, and months to years, with those categories roughly tracking with functional status. These ranges, along with an explanation from the physician about the difficulty of prognosticating, can often give families sufficient guidance with which to make important decisions. However, interpretation of a given prognosis may vary with the patient and family. One study that gave surrogate decision makers in the ICU hypothetical physician statements about prognosis and asked them to interpret them showed that surrogates tended to be optimistic, especially with worse prognoses.¹¹⁷

DISEASE TRAJECTORIES

Most disease trajectories can be included in one of the following functional categories: sudden extreme disability or near death; a period of good functionality, followed by

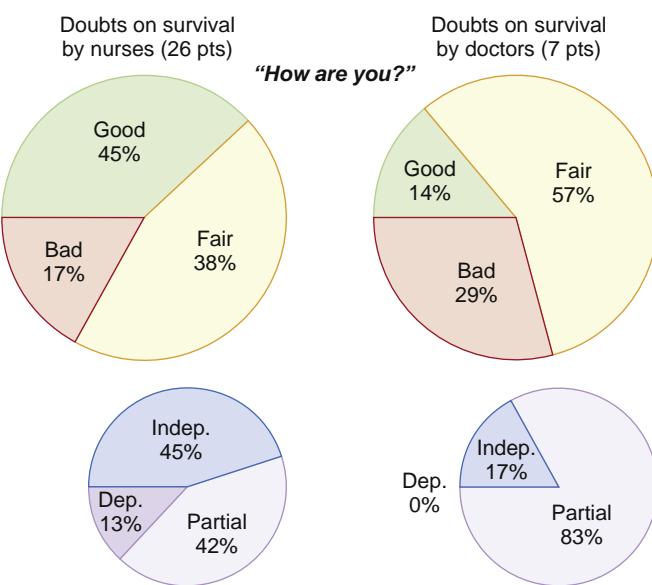


Fig. 52.8 Answers of survivors 6 months after being discharged from the intensive care unit for whom treatment had been considered futile or questionable by nurses or physicians to improve survival. *Dep.*, Dependent; *Indep.*, independent. (From Frick S, Uehlinger DE, Zuercher Zenklusen RM. Medical futility: predicting outcome of intensive care unit patients by nurses and doctors—a prospective comparative study. *Crit Care Med.* 2003;31:456–461.)

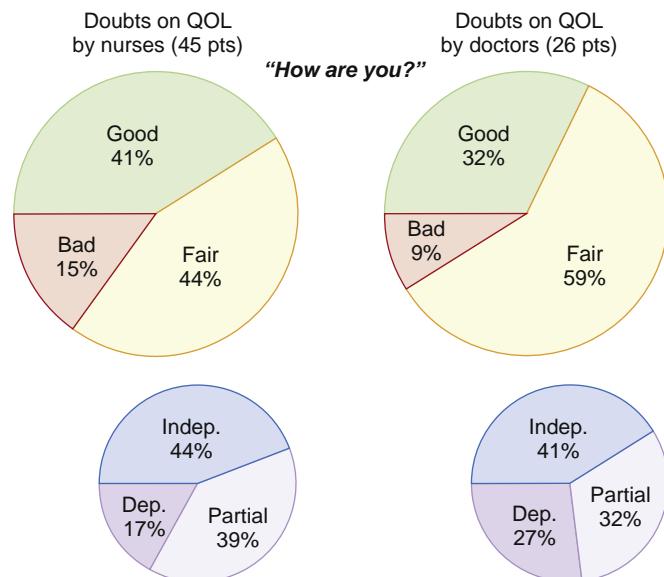


Fig. 52.9 Answers of survivors 6 months after being discharged from the intensive care unit for whom treatment had been considered futile or questionable by nurses or physicians to improve the quality of life (QOL). *Dep.*, Dependent; *Indep.*, independent. (From Frick S, Uehlinger DE, Zuercher Zenklusen RM. Medical futility: predicting outcome of intensive care unit patients by nurses and doctors—a prospective comparative study. *Crit Care Med.* 2003;31:456–461.)

a rapid, steady decline; a waxing and waning course with periods of decompensation followed by improvements; and a slow decline, starting at a low functional level (Fig. 52.10).¹¹⁹ These frameworks can be useful when discussing prognoses with patients, particularly in talking to patients with conditions that are difficult to predict such as COPD and CHF.

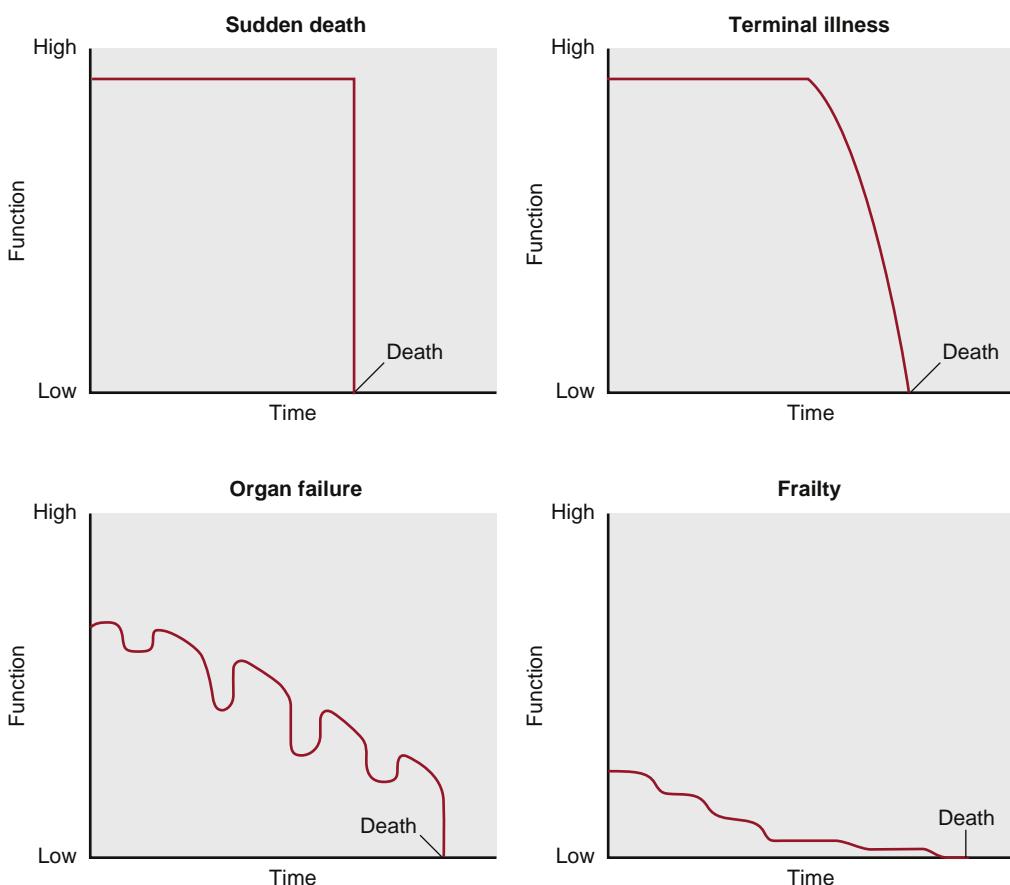


Fig. 52.10 Trajectories of dying. (From Lunney JR, Lynn J, Hogan C. Profiles of older Medicare decedents. *J Am Geriatr Soc*. 2002;50:1108–1112.)

PROGNOSTIC TOOLS

Multiple web-based prognostic tools exist, but they are typically specific to particular cancers. But an important consideration is that the type of cancer is actually less important than a variety of patient factors (e.g., functional status and laboratory values) as the disease becomes more advanced (Fig. 52.11).¹²⁰ In general, a patient with cancer who spends more than half of the day in bed has a median survival of 6 months (Box 52.5).¹²¹

Multiple tools, which are covered in depth in Chapter 84, have been proposed to help the clinician predict mortality in the ICU. These tools may be more useful in the research setting than for prediction of outcome in an individual patient.

Many conditions have courses that are difficult to predict. Table 52.2 gives characteristics associated with noncancer patients such as heart failure, dementia, hepatic cirrhosis, and COPD, with a median survival of 6 months or less,¹²² although it should be noted that the prognostic accuracy of these factors is not known.

Congestive Heart Failure

CHF often has a waxing and waning course. The Seattle Heart Failure Model estimates mean 1- to 3-year survival but does not appear to be able to predict whether individual patients are in the last year of life.¹²³ Factors associated with a poor prognosis include hospitalization, tachycardia, hypotension, decreased ejection fraction, and increased creatinine level.¹²⁴ In patients

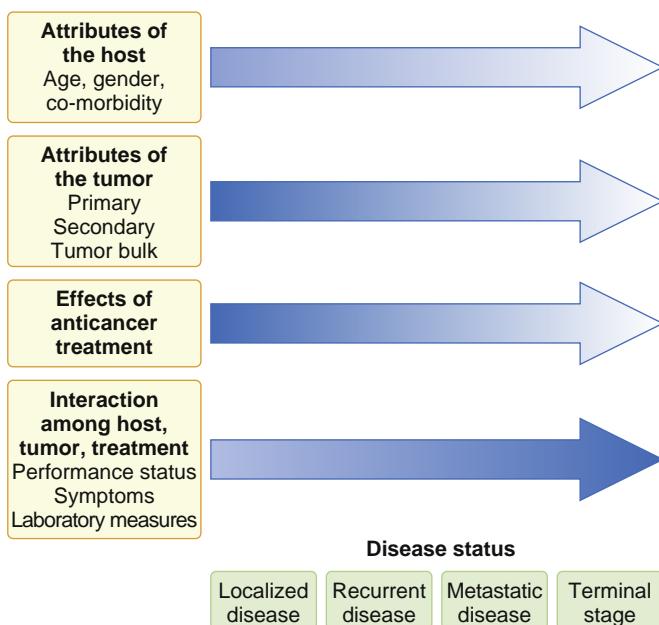


Fig. 52.11 Factors associated with the length of survival in patients with cancer. Depth of shading represents relative importance of the factor as a predictor of subsequent survival. (From Hauser CA, Stockler MR, Tattersall MH. Prognostic factors in patients with recently diagnosed incurable cancer: a systematic review. *Support Care Cancer*. 2006;14:999–1011.)

BOX 52.5 Cancer Presentations with a Median Survival of 6 Months or Less

Solid Cancers in General

Any locally advanced or metastatic solid cancer with one or more of the following presentations:

- Patient spends more than one half of the day in bed
- Serum calcium > 11.2 mg/dL
- Episode of extremity venous thromboembolism or pulmonary embolism
- Two or more brain metastases plus intracranial metastases
- Spinal cord compression with decreased ability to walk
- Malignant pericardial effusion

Carcinoma of Unknown Primary Origin

Any metastatic adenocarcinoma or undifferentiated carcinoma of unknown primary origin with one or more of the following presentations:

- Patient is ambulatory and can care for him or herself but cannot work
- Hepatic, bone, or adrenal metastases
- Recurrence of disease after chemotherapy
- Serum albumin < 3.5 mg/dL or weight loss of ≤ 10% in 6 months

Modified from Salpeter SR, Malter DS, Luo EJ, et al. Systematic review of cancer presentations with a median survival of six months or less. *J Palliat Med*. 2012;15:175–185.

hospitalized for acute decompensation of heart failure, older age and COPD were associated with decreased 1-year survival.¹²⁵

Dementia

The course of dementia is difficult to predict, and a patient's 6-month mortality is higher once the patient develops the common problems of infection and an inability to eat.¹²⁶ Probability of death within 6 months increases with advancing age, shortness of breath, immobility, and insufficient oral intake, among other presentations.¹²⁷

Chronic Obstructive Pulmonary Disease

The BODE Index, which is used to predict the risk of death in COPD, measures **body mass index**, airflow **obstruction**, **dyspnea**, and **exercise capacity**¹²⁸; however, its use of a 6-minute exercise capacity test makes it impractical for the bedside anesthesiologist. More than 3 days of mechanical ventilation and an inability to extubate the trachea successfully suggest a poor prognosis.¹²⁹

Liver Disease

In decompensated liver disease, the Model for End-Stage Liver Disease score is often used to predict a prognosis.¹³⁰ Hepatic encephalopathy and hepatorenal syndrome are also predictors of a poor prognosis.^{130,131}

Renal Disease

Patients with chronic kidney disease on dialysis will live 16% to 33% as long as age- and sex-matched patients who are not on dialysis.¹³² Probability of survival at 10 years for patients on dialysis who are older than 65 years of age is 3.1%.¹³² Poor functional and nutritional status, as well as comorbid conditions, suggest a poor prognosis.¹³²

Withdrawal of dialysis accounts for up to 20% of deaths in patients on dialysis each year, and the average patient lives 8 to 12 days after dialysis withdrawal.¹³³

SYMPTOM MANAGEMENT

Alternative Routes of Drug Delivery

Many patients near the end of life are unable to swallow oral medications as a result of oral lesions, nausea, the dying process, or other reasons. Many patients in palliative and hospice care have difficult intravenous access as a result of frequent medical care, dehydration, or other issues. To avoid multiple attempts at intravenous cannulation, palliative medicine practitioners and most hospices use subcutaneous infusions for the delivery of medications, especially opioids.^{136,137} An assumption of safety is based, in part, on studies showing that many intramuscular injections are actually administered into the subcutaneous tissue.¹³⁸ In addition, other types of drugs such as benzodiazepines, some antiemetic medications, antibiotics, neuroleptics, and even fluids can be subcutaneously administered in the palliative care setting.^{136,137,138a} While the subcutaneous administration of opioids is safe, the optimal conversion ratio from one route to another is a subject of debate.¹³⁹ Other studies support the transmucosal, sublingual, and rectal administration of opioids.¹³⁹ Finally, neuraxial drug delivery via continuous epidural infusions or intrathecal pumps can be utilized, particularly for intractable pain.^{139a}

Pain

Pain management in patients who are seriously ill can be quite different from other patients with pain. Some of these patients have pain that is best managed by a pain management specialist, and some will need adjuvant medications (Table 52.3). In cancer patients, 15% to 90% with solid tumors have pain, depending on the type and stage of cancer, as well as the age, race, and sex of the patient.¹⁴⁴ Most cancer pain is due to the cancer itself, but approximately one fifth of patients develop pain related to the cancer treatment.¹⁴⁵ The majority of cancer pain can be managed with the WHO "Cancer Pain Stepladder."¹⁴⁶ Zech published a prospective study of 2118 cancer patients using this stepladder during which 76% of the patients received pain relief with minimal side effects.¹⁴⁶ However, pain management may be significantly more challenging for patients with advanced cancer. Sixty to 90% of this population report pain that significantly impacts function, mood, and sleep. Pain of this severity may benefit from more advanced techniques such as interventional pain medicine (see Chapter 51),^{146a,b} psychological interventions,¹⁴⁷ or palliative chemotherapy or radiation therapy.

Bone Pain

Breast, lung, kidney, and prostate cancers frequently metastasize to the bones.¹⁴⁸ Patients with metastatic disease can have both osteoblastic and osteolytic bony lesions leading to severe pain.¹⁴⁹ Multiple targets for bone pain are possible, but no clear consensus has been reached on the best treatment methods.¹⁵⁰ Hormonal therapy is effective in breast, prostate, and endometrial cancers. Interventional techniques such as intrathecal catheters

TABLE 52.2 Presentations of Noncancer Diagnoses With a Median Survival of 6 Months or Less

Diagnosis	Presentation
HEART FAILURE	<ul style="list-style-type: none"> Hospitalization for moderate-to-severe symptomatic heart failure, NYHA Class III or IV, with three or more of the presentations listed. Age >70 years LVEF ≤20% Serum BNP > 950 pg/mL Cardiac troponin I > 0.4 ng/mL CRP >3.5 mg/L Fourth hospitalization for heart failure or repeat hospitalization within 2 months Dependency for two or more activities of daily living or need for home care after hospital discharge Weight loss ≤2.3 kg within 2 months, or serum albumin < 2.5 g/dL History of cardiogenic shock, ventricular or supraventricular arrhythmia, cardiac arrest, CPR, or mechanical ventilation Systolic blood pressure < 110 mm Hg Serum creatinine > 2 mg/dL or BUN > 40 mg/dL Serum sodium < 135 mEq/L Peripheral vascular disease or cerebrovascular disease Other comorbid illness, such as diabetes mellitus, dementia, COPD, cirrhosis, and cancer, among others
DEMENTIA	<ul style="list-style-type: none"> Advanced dementia with dependency in all activities of daily living, bedbound status, urinary and bowel incontinence, decreased ability to communicate verbally, and admission to a hospital or skilled nursing facility with one or more of the presentations listed. BMI < 18.5 kg/m², decreased oral intake, or significant weight loss Presence of at least one pressure ulcer Evidence of at least one comorbid illness Male sex plus > 90 years of age Placement of a feeding tube attributable to inability to eat or history of aspiration
HEPATIC CIRRHOSIS	<ul style="list-style-type: none"> Decompensated hepatic cirrhosis and one or more of the presentations listed. MELD score ≥21
Decompensated hepatic cirrhosis with hospitalization for an acute illness related to liver disease and one or more of the presentations listed.	<ul style="list-style-type: none"> MELD score ≥18 Hospitalization in an intensive care unit related to severe decompensation of liver disease with hypotension requiring the use of pressors, serum creatinine > 1.5 mg/dL, or evidence of jaundice Evidence of hepatopulmonary syndrome or rapidly progressive hepatorenal syndrome
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	<ul style="list-style-type: none"> Hospitalization for a severe COPD exacerbation, with $\text{PaO}_2 \leq 55$ mm Hg, $\text{PaCO}_2 \geq 50$ mm Hg, and supplemental oxygen dependence, with three or more of the presentations listed. Age >70 years Evidence of right-sided heart failure Repeat hospitalization for COPD within 2 months History of intubation and mechanical ventilation Required considerable assistance and frequent medical care and/or dependence for three or more activities of daily living before hospitalization Need for home care after hospital discharge Malnutrition (weight loss of ≥ 2.3 kg, serum albumin < 2.5 g/dL or BMI < 18 kg/m²) Serum creatinine > 2 mg/dL

BMI, Body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; CRP, C-reactive protein; LVEF, left ventricular ejection fraction; MELD, Model for End-Stage Liver Disease; NYHA, New York Heart Association; PaCO_2 , partial arterial pressure of carbon dioxide; PaO_2 , partial arterial pressure of oxygen. Modified from Salpeter SR, Luo EJ, Malter DS, et al. Systematic review of noncancer presentations with a median survival of 6 months or less. *Am J Med*. 2012;125:512 e1–6.

TABLE 52.3 Adjuvant Analgesics in the Management of Cancer Pain

	Examples	Comment
MULTIPURPOSE ANALGESICS		
Glucocorticoids	Dexamethasone, prednisone	Are used for bone pain, neuropathic pain, lymphedema pain, headache, and bowel obstruction
ANTIDEPRESSANTS		
TCAs	Desipramine, amitriptyline	Are used for opioid-refractory neuropathic pain; often used with comorbid depression; secondary amine compounds (e.g., desipramine) have fewer side effects and might be preferred
SNRIs	Duloxetine, milnacipran	Good evidence exists for their use in some conditions but are overall less effective than TCAs; better side-effect profile than TCAs and are often tried first
SSRIs	Paroxetine, citalopram	Evidence for their use is scarce; if pain is the target, then other subclasses are preferred

TABLE 52.3 Adjuvant Analgesics in the Management of Cancer Pain—cont'd

Other	Bupropion	Little evidence exists for its effectiveness but less sedating than other antidepressants; is often tried early when fatigue or somnolence is a problem
α_2 -Adrenergic agonists	Tizanidine, clonidine	Are seldom used systemically because of side effects, but tizanidine is preferred for a trial; clonidine is used in neuraxial analgesia
Cannabinoid	THC/cannabidiol, nabilone, THC	Good evidence exists for THC/cannabidiol when used in cancer pain; evidence is scarce for other commercially available compounds
TOPICAL AGENTS		
Anesthetic	Lidocaine patch, local anesthetic creams	Sometimes used in localized pain
Capsaicin	8% patch; 0.25%-0.75% creams	High concentration patch is indicated for postherpetic neuralgia
NSAIDs	Diclofenac and others	Evidence exists for their use in focal musculoskeletal pains
TCA	Doxepin cream	Is used in treating itching; can be tried for pain
Others		Compounding creams with various drugs have been empirically tried, but no evidence exists for effectiveness
USED FOR NEUROPATHIC PAIN		
Multipurpose drugs	As above	As above
ANTICONVULSANTS		
Gabapentinoids	Gabapentin, pregabalin	Are used first for opioid-refractory neuropathic pain unless comorbid depression; may have multipurpose uses in view of the evidence in postsurgical pain; both drugs act as N-type calcium channel blockers in the CNS, but individuals vary in response to one or the other
Others	Oxcarbazepine, lamotrigine, topiramate, lacosamide, valproate, carbamazepine, phenytoin	Evidence is scarce for all drugs listed; newer drugs are preferred because of reduced side-effect liability, but individual variation is great; all drugs are considered for opioid-refractory neuropathic pain if antidepressants and gabapentinoids are ineffective
SODIUM-CHANNEL DRUGS		
Sodium-channel blockers	Mexiteline, intravenous lidocaine	Good evidence exists for intravenous lidocaine
Sodium-channel modulator	Lacosamide	New anticonvulsant with very scarce evidence of analgesic effects
GABA AGONISTS		
GABA _A agonist	Clonazepam	Evidence is scarce but used for neuropathic pain with anxiety
GABA _B agonist	Baclofen	Evidence for the treatment of trigeminal neuralgia is the basis for trials in other types of neuropathic pain
N-methyl-D-aspartate inhibitors	Ketamine, memantine, and others	Evidence is scarce for ketamine, but experience is positive with intravenous use in advanced illness or pain crisis; little evidence exists for oral drugs
USED FOR BONE PAIN		
Bisphosphonates	Pamidronate, ibandronate, clodronate	Good evidence exists for their use; similar to NSAIDs or glucocorticoids, usually considered first-line treatment; also reduces other adverse skeletal-related events; concern about osteonecrosis of the jaw and renal insufficiency might restrict its use
Calcitonin		Evidence is scarce but is usually well tolerated
Radiopharmaceuticals	Strontium-89, samarium-153	Evidence is good, but their use is restricted because of bone-marrow effects and the need for expertise
USED FOR BOWEL OBSTRUCTION		
Anticholinergic drugs	Hyoscine compounds, glycopyrionium	Along with a glucocorticoid, are considered first-line adjuvant treatments for nonsurgical bowel obstruction
Somatostatin analog	Octreotide	Along with a glucocorticoid, is considered a first-line adjuvant treatment for nonsurgical bowel obstruction

CNS, Central nervous system; GABA, gamma-aminobutyric acid; NSAIDs, nonsteroidal antiinflammatory drugs; SNRIs, selective noradrenaline reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; THC, tetrahydrocannabinol. Modified from Portenoy RK. Treatment of cancer pain. *Lancet*. 2011;377:2236-2247.

may be appropriate in some patients.¹⁵¹ Palliative radiotherapy can be helpful for patients with bone metastases, although pain relief may take several weeks.¹⁵² Dexamethasone orally, subcutaneously, or intravenously is

commonly recommended for bone pain by expert consensus, although only a few small studies support its use.¹⁵⁴ Bone-modifying agents, such as zoledronic acid or pamidronate, have shown benefit for bony pain in some cancers

and should be considered when appropriate from an oncologic standpoint.^{148,155} Nonsteroidal antiinflammatory drugs are helpful in alleviating cancer pain, although their advantage when combined with opioids is less clear.¹⁵⁶ More advanced interventions such as epidural steroid injections, vertebroplasty/kyphoplasty, or surgery may be indicated.^{156a}

Neuropathic Pain

Between 17% and 28% of patients with advanced cancer have neuropathic pain.¹⁵⁷ More information on neuropathic pain, the use of lidocaine and ketamine, and other adjuvant medications is available in **Chapters 25 and 51** (see **Table 52.3**). As always, a patient's life expectancy should be considered, because some medications may be difficult to titrate adequately in a short period.

Pain in the Intensive Care Unit

In the ICU, pain is common and attributable to many factors such as surgical wounds, placement of invasive monitoring devices, and immobility.¹⁵⁸ Pain is also difficult to assess in the ICU because the trachea is intubated or the patient is unable to speak. The Behavioral Pain Scale¹⁵⁹ and the Critical Care Pain Observation Tool¹⁶⁰ are validated methods of assessing pain in the ICU population.¹⁶¹ Commonalities among the tools include assessment of facial expression, body movement, and synchrony with ventilation. In the SUPPORT trial, pain was poorly controlled among those who died in the hospital, with half of the surrogates indicating that their family member had moderate-to-severe pain for at least half of the time in the 3 days before death.¹⁴ Fortunately, a more recent study has demonstrated improved pain assessment and treatment in the ICU.¹⁶²

OPIOID USE

Opioid use at the end of life is common, although consumption dramatically varies throughout the world.¹⁹ In a 2012 study of 1068 patients at six U.S. medical centers, 70% of patients received an opioid in the last week of life, and 47% received opioids in the last 24 hours.¹⁶³ Some physicians are hesitant to use opioids at the end of life for fear of hastening a patient's death. A study by Morita in 2001 retrospectively analyzed opioid and sedative consumption of 209 patients in the 48 hours before death and found no difference in survival based on opiate or sedative dose.¹⁶⁴ A small study on the rate of increase of opioids found no correlation with time to death, although total morphine doses were relatively low overall in the study.¹⁶⁵ A larger study by Portenoy in 2006 showed a weak association with total opioid dose and time to death, but this association appeared to account for less than 10% of the variance even when combined with other variables.¹⁶⁶ Most experts believe that appropriately administered opioids do not hasten death, can be safely used, and generally do not require invoking the doctrine of double effect.¹⁶⁷ Some authors have urged caution with the use of opioids in patients with cancer and uncertain prognoses to decrease the risk of opioid dependence and abuse in patients with the possibility of a long life after treatment,¹⁶⁸ but overall,

opioids should be titrated based on the clinician's assessment of the pain.

Interventional Pain Management at the End of Life

Despite the guidance provided by the WHO Stepladder,^{168a} 10% to 20% of cancer patients have pain that is refractory to parenteral management.^{168b,c} Select patients may benefit from interventional pain modalities.^{156a} However, patients at the end of life may be more prone to bleeding from coagulopathy or thrombocytopenia and infection from immunosuppression. These issues need to be evaluated carefully by an interventional pain specialist. Abdominal pain, especially for pancreatic cancer, can be treated with celiac plexus blocks or neurolysis, while pelvic pain may be addressed with superior hypogastric blocks or neurolysis. These techniques are described in detail in **Chapter 51**. Less invasive modalities such as peripheral nerve blocks or trigger point injections may also be beneficial.

Neuraxial (i.e., intrathecal and epidural) analgesia can decrease numerical pain scores while significantly decreasing oral opioid intake, which may lead to fewer side effects such as constipation and sedation.^{139a} In a randomized controlled trial of 202 patients with refractory cancer pain comparing comprehensive medical management versus an implantable intrathecal drug delivery system, those in the intrathecal group had significant reductions in fatigue and depressed level of consciousness. Additionally, this study showed a trend toward improved survival, with 53.9% of patients receiving intrathecal analgesia remaining alive at 6 months compared with 37.2% of the control group ($P = .06$).^{168d}

NAUSEA AND VOMITING

Nausea and vomiting are common complaints in the palliative care and hospice populations and cause significant distress for patients and families.¹⁶⁹ Many techniques and medications used in the treatment of nausea and vomiting are similar to those used in the perioperative period. As with every patient, the first step in treating nausea and vomiting is a thorough evaluation of possible causes (**Fig. 52.12**). The following section highlights issues specific to patients with life-limiting diseases.

Nausea and Vomiting Related to Chemotherapy and Radiation Therapy

Many patients undergoing chemotherapy experience anticipatory nausea and vomiting. The 2011 American Society of Clinical Oncology Practice Guidelines for chemotherapy and radiation therapy include the prescription of a 5-hydroxytryptamine-3 antagonist, such as ondansetron, often with dexamethasone, and the addition of a neurokinin-1 antagonist, such as aprepitant, for the most emetogenic chemotherapy regimens.¹⁷⁰ Benzodiazepines may also be beneficial. For nonchemotherapy-related or radiation therapy-related nausea and vomiting, no Level 1a or 1b evidence is currently available to guide decisions on the choice of an antiemetic agent in the palliative care population. Unlike routine postoperative nausea and vomiting, patients may benefit from scheduled antiemetics with additional medications as needed.

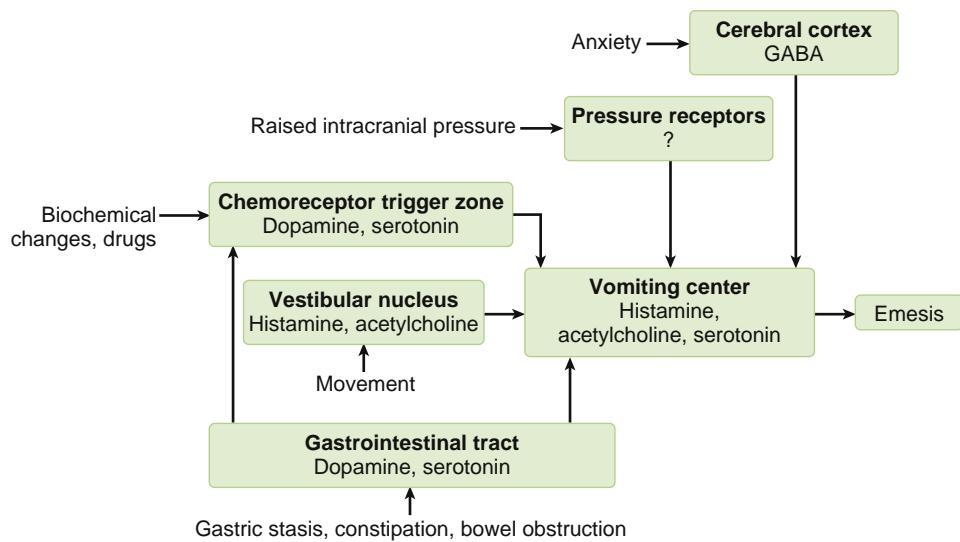


Fig. 52.12 Causes of nausea and vomiting. GABA, Gamma-aminobutyric acid. (From Gupta M, Davis M, LeGrand S, et al. Nausea and vomiting in advanced cancer: the Cleveland Clinic protocol. *J Support Oncol*. 2013;11:8–13.)

BOWEL OBSTRUCTION

Some patients with abdominal tumors may develop partial or complete bowel obstruction. First-line therapy consists of medical management, often with steroids and octreotide.¹⁷¹ Surgical outcomes for patients with bowel obstruction and a life expectancy of less than 2 months are poor,¹⁷² and gastrointestinal stents should be considered. Placement of a nasogastric tube should be considered for immediate relief while other options are considered. A venting gastrostomy tube is an option in patients who are refractory to treatment and can allow the patients to enjoy the taste of food while allowing gastric decompression.

ARTIFICIAL HYDRATION AND NUTRITION

Many patients receiving palliative care are unable to take in food or fluids because of nausea, dysphagia, or obstruction. The decision of whether to administer artificial hydration and nutrition is often a difficult one for patients and physicians. Both parties may hold strong cultural or religious views, and many describe a fear of “starving” the patient.¹⁷³ Symptoms of hunger are less common in advanced disease, and thirst can be treated with ice chips or mouth swabs.¹⁷⁴ The administration of artificial hydration and nutrition is associated with risks of fluid overload leading to choking or edema, as well as diarrhea and nausea.¹⁷⁵ Additional risks associated with a gastrostomy tube include dislodgement and the possible increased need for restraints.¹⁷⁵ The administration of enteral or parenteral nutrition and hydration is considered a medical intervention, and, as such, the risks and benefits should be discussed with patients and families.¹⁷³ The benefit of artificial hydration and nutrition has been established for patients in a persistent vegetative state or those with acute stroke or head injury, short-term critical illness, oropharyngeal cancers, and possibly bulbar amyotrophic lateral sclerosis.¹⁷⁶ Additionally, artificial hydration may improve symptoms of delirium in patients with cancer, although it does not influence survival in most

advanced cancers.¹⁷⁷ The use of percutaneous feeding tubes in patients with advanced dementia does not prevent pneumonia or improve survival and is not recommended.^{178,179} For some patients, a time-limited trial of artificial hydration or nutrition may be appropriate to evaluate for benefit, such as improvement in delirium, while monitoring for side effects.

DYSPNEA

Dyspnea is “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity,”¹⁸⁰ as differentiated from breathing that appears labored or fast to an observer. Dyspnea is common in patients with a high risk of death^{182,183} and was identified as the most distressing symptom by patients who could self-report in the ICU, regardless of their mechanical ventilation status.¹⁸⁴ Dyspnea increases closer to the time of death, even in patients without known cardiopulmonary disease.¹⁸⁵ Treatment is either aimed at reversing the cause of dyspnea (e.g., thoracentesis for an effusion) or at symptom management. Nonpharmacologic therapy such as a fan or pulmonary rehabilitation may be helpful.¹⁸⁶ Studies of low-dose opioids in patients with refractory dyspnea support their safety and efficacy.^{187,188} A randomized, double-blind, crossover study of 48 COPD patients who were taking 20 mg of sustained-release morphine daily showed a significant improvement in dyspnea with minimal side effects.¹⁸⁹ Studies of the effect of benzodiazepines with and without opioids for dyspnea are small and mixed, with a trend toward possible benefit.¹⁹⁰⁻¹⁹²

DEPRESSION AND ANXIETY IN THE PATIENT RECEIVING PALLIATIVE CARE

Depression and anxiety are common at the end of life, with estimates ranging from 5% to 30% and 7% to 13%, respectively.¹⁹⁸ Many factors contribute to psychological distress, including social, economic, spiritual, and

TABLE 52.4 Distinguishing Characteristics of Grief and Depression in Patients Who Are Terminally Ill

Characteristic	Normal Grief	Depression
Nature of response	Adaptive	Maladaptive
Focus of distress	In response to a particular loss; not affecting all aspects of life	Pervasive; affecting all aspects of life
Symptom fluctuations	Symptoms coming in waves, generally improving with time	Constant
Mood	Sadness and dysphoria	Protracted and constant depression or flat affect
Interests and capacity for pleasure	Interests and capacity for pleasure remaining intact; diminishing engagement in activities because of functional decline	Anhedonia with significant diminished interest or pleasure in all activities
Hope	Episodic and focal loss of hope; hopes possibly changing over time; giving positive orientation toward the future	Persistent and pervasive hopelessness
Self-worth	Maintaining self-worth, although with feelings of helplessness	Worthlessness with the belief that one's life has no value
Guilt	Regrets and guilt over specific events	Excessive feelings of guilt
Suicidal ideation	Passive and fleeting desire for a hastened death	Preoccupation with a desire to die

From Widera EW, Block SD. Managing grief and depression at the end of life. *Am Fam Physician*. 2012;86:259–264.

physical stressors associated with serious illness.¹⁹⁹ A rapid screening test for depression consisting of two questions, “Are you depressed?” and “Have you experienced a loss of interest in things or activities you would normally enjoy?” has a sensitivity of 91% and a specificity of 68% and has been validated in the palliative care population.²⁰⁰ Patients who screen positive for depression or who have suicidal or homicidal ideations should be referred to a psychiatrist or other experienced provider. Depression should be distinguished from delirium and normal grief (Table 52.4).²⁰¹ For the anesthesiologist, recognizing depression and making appropriate referrals is important.

Treatments for depression vary by life expectancy. Selective serotonin reuptake inhibitors and monoamine oxidase inhibitors may be appropriate for patients with a longer life expectancy, since the time to onset is 1 to 2 months. For patients with a life expectancy of weeks to a few months, methylphenidate has been well studied in the cancer population. The onset of action is 1 to 3 days and is generally effective and well-tolerated for depression and fatigue.^{202,203}

DELIRIUM AT THE END OF LIFE

Delirium is covered in depth in Chapter 65. It affects 28% to 88% of patients who are terminally ill, with increasing incidence as death approaches.^{204,205} The Confusion Assessment Method has been validated in the palliative care population.^{206,207} Some patients may have more than one possible cause of delirium (Box 52.6). Delirium can have a major impact on a patient’s ability to make a well-informed decision about treatment options, including surgery, which may have ethical and legal implications. Most patients who recover remember being delirious, and those who do find it very distressing.²⁰⁸

As much as half of the delirium near the end of life may be reversible.²⁰⁵ Increased likelihood of reversible delirium

BOX 52.6 Causes of Delirium

Metabolic disturbance
Hypercalcemia
Hyponatremia
Hypernatremia
Dehydration
Glycemic derangements
Organ failure
Renal failure
Liver failure
Respiratory failure
Medications
Opioids
Benzodiazepines
Anticholinergic agents
Steroids
Sepsis
Pneumonia
Urinary tract infection
Brain pathologic conditions
Tumor
Metastases
Leptomeningeal disease
Nonconvulsive status epilepticus
Hypoxia
Withdrawal
Alcohol
Benzodiazepines
Hematologic conditions
Disseminated intravascular coagulation
Anemia

From LeGrand SB. Delirium in palliative medicine: a review. *J Pain Symptom Manage*. 2012;44:583–594.

is associated with a younger age, less severe impairment, and lack of organ failure.²⁰⁹ Patients with true terminal delirium have a very short life expectancy.²⁰⁴ Attempts at workup should be based on the patient’s goals of care (Box 52.7). For example, the family of a cancer patient

BOX 52.7 Evaluation of Delirium

- Determining the goals of care
- Reviewing medications
- Considering the possibility of withdrawal
- Identifying any hematologic or metabolic abnormalities or organ failure
 - Complete metabolic panel
 - Complete blood count
- Evaluating oxygen levels
 - Oxygen saturation
- Identifying infections
 - Urine culture
 - Blood cultures
 - Chest x-ray imaging
- Performing specialized testing, if appropriate
 - Electroencephalogram
 - Arterial blood gas
 - Tests for disseminated intravascular coagulation
 - Test for thyroid-stimulating hormone
 - Computed tomography scan or magnetic resonance imaging scan of the brain
 - Lumbar puncture

From LeGrand SB. Delirium in palliative medicine: a review. *J Pain Symptom Manage*. 2012;44:583–594.

who develops delirium but previously had an acceptable quality of life may desire a workup for potential reversible causes (e.g., urinalysis, chest x-ray study, or brain imaging), whereas the family of a patient who had previously been nearly comatose and expected to die in hours to days may not want to subject their family member to further workup.

Although delirium is often associated with agitation, hypoactive delirium, during which a patient may have decreased interaction with the environment and exhibit inattention, is likely more common than most clinicians appreciate.²¹⁰ Hypoactive delirium is considered disturbing by patients who experience it, but no consensus has been reached on whether or how to treat hypoactive delirium.²¹¹

While delirium is treated similarly for palliative care patients as it is for medical and surgical inpatients, there is inadequate evidence for specific recommendations on management of delirium in the palliative care settings.^{211a} Conventional and atypical antipsychotics can both be used to treat delirium in palliative care.^{211a} Some patients may ultimately require palliative sedation to treat terminal delirium.

BLEEDING IN THE PATIENT RECEIVING PALLIATIVE CARE

Bleeding can be caused by numerous pathologic conditions, including coagulation disorders and cancers. Fibrinolytic inhibitors such as tranexamic acid, interventional radiologic procedures such as embolization, and surgery have been suggested for patients with compatible goals and life expectancy.²¹² Exsanguination in patients receiving palliative care is uncommon but can be upsetting to patients, families, and providers. No randomized trials of best treatments have been conducted. Some practical suggestions include the use of dark towels, suction, holding pressure,

and staying with the patient. Medications such as benzodiazepines, opioids, and ketamine are frequently suggested during exsanguination to provide sedation and amnesia.²¹³

The Dying Process

Most physicians have observed people die but may not have witnessed the dying process. Over 500,000 people die in the ICU every year in the United States alone, and more die after an ICU stay.^{213a} Understanding the dying process is important because family members may ask physicians what the dying process will be like for the patient. Anesthesiologists need to be able to recognize the signs that a patient is imminently dying.

The variation in the timing with which a patient develops many symptoms is substantial, with 84% of patients being drowsy or comatose 24 hours before death, and acrocyanosis and the loss of a radial pulse occurring a median of 1 hour before death^{213b} (Table 52.5). Some of the most noticeable symptoms will be cessation of oral intake, lack of responsiveness, and a build-up of oral and tracheal secretions leading to gurgling, sometimes called the “death rattle.” Terminal secretions are thought to be from the airway or oropharynx that cannot be cleared because of the inability to cough or swallow.^{213c} Despite widespread clinical use of antimuscarinic drugs for terminal secretions, strikingly few studies support this practice. A large study comparing atropine, hyoscine butylbromide, and scopolamine showed improvement in symptoms but no difference among those agents.^{213d} A study using sublingual atropine versus placebo showed no difference.^{213e} Of note, many of these small studies have multiple methodologic limitations. Family members differ in their interpretations of the sound, with some but not all finding it unsettling.^{213f} Many clinicians believe the noisy breathing is not bothersome to patients because most are generally unconscious, although evidence to support this view is lacking.

WITHDRAWAL OF LIFE SUPPORT

Some patients or family members may wish to discontinue mechanical ventilation or other forms of life support. Withdrawal of life support is ethically acceptable and respects patient autonomy. Anesthesiologists can provide expertise in the management of pain and anxiety with the withdrawal of ventilation. Multiple protocols using an opioid for pain or dyspnea and a benzodiazepine for agitation or anxiety are available in the ICU for withdrawal of ventilatory support.^{213g} Interestingly, studies of protocolized life support withdrawal have not demonstrated an improvement in provider perception of the quality of death.^{213h,i} A pilot study evaluating the effect of the use of a protocol to guide withdrawal of life support suggested that while symptoms are generally well-controlled around the time of extubation, areas in need of improvement include documentation of family meetings and provision of emotional or spiritual support to families and staff members.^{213j} This study highlights the need to devote specific attention to the nonsymptomatic needs of patients and families near the time of death, including making arrangements for rituals and family support, and involving a spiritual advisor for some families.^{213g}

TABLE 52.5 Changes During the Dying Process

Changes	Exhibited Signs
Fatigue, weakness	Decreasing function Decreasing attention to hygiene Inability to move around the bed Inability to lift head off the pillow
Cutaneous ischemia	Erythema over bony prominences Skin breakdown Wounds
Pain	Facial grimacing Tension in forehead and between eyebrows
Decreasing food intake, wasting	Anorexia Poor intake Aspiration, asphyxiation Weight loss, muscle, and fat loss notable in temples
Loss of ability to close eyes	Eyelids not closed Whites of eyes show (with or without pupils visible)
Decreasing fluid intake, dehydration	Poor intake Aspiration Peripheral edema attributable to hypoalbuminemia Dehydration, dry mucous membranes or conjunctivae
Cardiac dysfunction, renal failure	Tachycardia Hypertension followed by hypotension Peripheral cooling Peripheral and central cyanosis (bluing of extremities) Mottling of the skin (livedo reticularis) Venous pooling along dependent skin surfaces Dark urine Oliguria, anuria
Neurologic dysfunction, including: Decreased level of consciousness	Increased drowsiness Difficulty awakening Nonresponsive to verbal or tactile stimuli
Decreased ability to communicate	Difficulty finding words Monosyllabic words, short sentences Delayed or inappropriate responses Not verbally responsive
Respiratory dysfunction	Change in ventilatory rate—increasing first, then slowing Decreasing tidal volume Abnormal breathing patterns—apnea, Cheyne-Stokes respirations, agonal breaths Loss of ability to swallow Dysphagia Coughing, choking Loss of gag reflex Buildup of oral and tracheal secretions Gurgling
Loss of sphincter control	Incontinence of urine or bowels Maceration of skin Perineal candidiasis Terminal delirium Early signs of cognitive failure, (e.g., day-night reversal) Agitation, restlessness Purposeless, repetitious movements Moaning, groaning
Rare, unexpected events	Bursts of energy just before death occurs, the “golden glow” Aspiration, asphyxiation

From Ferris FD. Last hours of living. *Clin Geriatr Med.* 2004;20:641–667, vi.

Outcomes of Withdrawal of Life Support

One study of 74 medical patients in an ICU who were expected to die shortly after extubation showed a mean morphine dose of 5.3 mg/h in the last hour of mechanical ventilation, followed by 10.6 mg/h during the hour before death.^{213k} The average time to death was 153

minutes after extubation, with a range of 4 to 934 minutes. Somewhat surprisingly, each 1 mg/h increase of morphine corresponded to an 8-minute delay in death.^{213k} This response is similar to an earlier study that showed a 13-minute increase in the time to death with each 1 mg/h increase of benzodiazepine.^{213l} Longer

time interval between initiation of withdrawal of life support to death has been associated with improved family satisfaction.^{213m}

Paralytic Drugs in the Withdrawal of Life Support

As noted in [Chapter 8](#), patients should not be paralyzed before extubation of the trachea; it obscures symptom assessment and may lead to patient suffering. Patients already on paralytic medications should await the return of neuromuscular function before extubation unless doing so causes undue burden on the patient.²¹³ⁿ

PEDIATRIC HOSPICE CARE AND PALLIATIVE CARE

Palliative care is appropriate for many children with chronic serious illnesses, and the WHO states that pediatric palliative care can be successfully delivered even in resource-limited settings.¹ Pediatric hospice and palliative care are similar to their adult counterparts, but the patient's developmental stage is incorporated into the pediatric care plan. Explanations of illness and death depend on the child's developmental stage. A child younger than 2 years of age has no concept of death, whereas a 10-year-old child may be interested in the details of the dying process.^{213o}

Characteristics of the Pediatric Palliative Care Population

The variety of diagnoses for patients in pediatric palliative care are wider than those for adults^{213p} with the most common disorders being congenital and neuromuscular in origin.^{213p} In the largest observational study to date, over one third of pediatric patients referred for palliative care consultation services were 1 to 9 years of age, one third were 10 to 18 years old, and less than 20% were younger than 1 year of age.^{213p} Children often have prolonged survival after the initial palliative care consultation compared to adults.^{213p} Some disorders, including chromosomal or severe developmental abnormalities, are rarely seen by adult palliative care physicians. The decision to forgo treatment with curative intent is generally difficult for families, and prognostication is similarly difficult for providers.^{213o} Moreover, multiple legal issues related to declining medical treatment in children exist that differ from those related to adults.^{213q}

Symptom Management in Pediatric Palliative Care

Historically, symptoms in children with serious illnesses have been poorly managed. In a retrospective survey of parents of deceased children, parents noted that their children suffered "a lot" or "a great deal," mostly from pain, fatigue, and dyspnea.^{213q} In contrast to most studies of adults near the end of life, a 2011 study noted neurologic symptoms being more prevalent,^{213p} suggesting a need for a better understanding and treatment of these symptoms in the pediatric population. Regional anesthesia has been reported as being of benefit to pediatric patients with pain that is difficult to manage with systemic treatment.^{213r} Data on specific therapies for children are limited, and many practitioners use medications based on adult studies.

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KEY POINTS

- Patients undergoing pulmonary resection 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).
- Patients with underlying lung disease have a decreased risk of respiratory complications when pulmonary resections are performed with video-assisted thoracoscopic surgery (VATS).
- After lung resection surgery, it is usually possible to wean and extubate patients with adequate predicted postoperative respiratory function in the operating room provided they are “AWaC” (alert, warm, and comfortable).
- Interventions that 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.
- Geriatric patients are at high risk for cardiac complications, particularly cardiac arrhythmias (see Chapter 65), after large pulmonary resections. Preoperative exercise capacity is the best predictor of postthoracotomy outcome in the older patient.
- The ability to perform fiberoptic bronchoscopy and a detailed knowledge of bronchial anatomy are necessary for anesthesiologists to provide reliable lung isolation.
- Use of double-lumen endobronchial tubes (DLTs) is the standard method of providing lung isolation in adults. Bronchial blockers are a reasonable alternative for lung isolation in patients with abnormal upper or lower airways.
- With the use of intravenous anesthetic techniques or volatile anesthetics at less than or equal to 1–minimum alveolar concentration (MAC) doses, hypoxemia during one-lung ventilation (OLV) occurs infrequently. The use of continuous positive airway pressure (CPAP) or positive end-expiratory pressure (PEEP) as treatment for hypoxemia during OLV should be guided by the individual patient’s lung mechanics.
- The use of large tidal volumes during OLV (e.g., 10 mL/kg) can contribute to acute lung injury, particularly in patients at increased respiratory risk, such as after pneumonectomy.
- The underlying principle of management of a patient with a bronchopleural fistula is to secure lung isolation before positive pressure ventilation repositioning the patient for surgery.
- Anesthetic management of a patient with an anterior or superior mediastinal mass should be guided by the patient’s symptoms, the preoperative computed tomography (CT) scan, and the echocardiography findings. The fundamental principle of anesthetic management for these patients is *noli ponti ignii consumere* (“don’t burn your bridges”).
- Continuous paravertebral local anesthetic blockade combined with multimodal analgesia is a reasonable alternative to epidural analgesia for thoracic surgery with fewer side effects.

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 evolved so have the anesthetic techniques to manage these patients. Thoracic surgery at the beginning of the last century was primarily for infectious indications (lung abscess, bronchiectasis, empyema). Although these cases still present for surgery in the postantibiotic era, now the most common indications are related to malignancies (pulmonary, esophageal, and mediastinal). In addition, the last

two decades have seen the beginnings of surgical therapy for end-stage lung diseases with procedures such as lung transplantation and lung volume reduction. Fundamental to anesthetic management for the majority of thoracic procedures are two techniques: (1) lung isolation to facilitate surgical access within the thorax, and (2) management of one-lung anesthesia. In this chapter, we initially discuss preanesthetic assessment for thoracic surgery, outline intraoperative management principles common to most thoracic surgical procedures, discuss specific anesthetic considerations in common and less common surgical operations, and we finish with a description of postoperative management issues in thoracic surgical patients.

PREOPERATIVE EVALUATION OF THE THORACIC SURGERY PATIENT (SEE CHAPTER 31)

Preoperative anesthetic assessment prior to chest surgery is a continually evolving science and art. Recent advances in anesthetic management, surgical techniques, and perioperative care have expanded the envelope of patients now considered to be “operable.”¹ This discussion focuses primarily on preanesthetic assessment for pulmonary resection surgery in cancer patients. However, the basic principles described will apply to all other types of nonmalignant pulmonary resections and to other chest surgery.

Although 87% of patients with lung cancer will die of their disease, the 13% cure rate represents approximately 26,000 survivors per year in North America. Surgical resection is responsible for essentially all of these cures. 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.

The patient is commonly assessed initially as an outpatient 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 to 15 minutes 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. Elements vital to each assessment are described.

An increasing number of thoracic surgeons are now being trained to perform “lung-sparing” resections such as sleeve-lobectomies or segmentectomies, and resections with minimally invasive techniques such as video-assisted thoracoscopic surgery (VATS) or robotic surgery. 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.

It is the anesthesiologist’s responsibility to use the preoperative assessment to identify 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. This is the primary function of the preanesthetic assessment. However, there are occasions when the anesthesiologist should contribute his or her opinion about 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. Prethoracotomy assessment naturally involves all of the factors of a complete anesthetic assessment: past history, allergies, medications, upper airway, and so on. This section concentrates on the additional

information, beyond a standard anesthetic assessment, that the anesthesiologist needs to manage a patient undergoing a pulmonary resection.

PERIOPERATIVE COMPLICATIONS

The major cause of perioperative morbidity and mortality in the thoracic surgical population is respiratory complications. Major respiratory complications—atelectasis, pneumonia, and respiratory failure—occur in 15% to 20% of patients and account for the majority of the expected 3% to 4% mortality.² For other types of surgery, cardiac and vascular complications are the leading cause of early perioperative morbidity and mortality. Cardiac complications such as arrhythmia and ischemia occur in 10% to 15% of the thoracic population.

ASSESSMENT OF RESPIRATORY FUNCTION

The best assessment of respiratory function comes from a detailed history of the patient’s quality of life. All patients undergoing a pulmonary resection should have baseline simple spirometry done preoperatively.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 health care team. Respiratory function can be divided into three related but somewhat independent areas: respiratory mechanics, gas exchange, and cardiopulmonary interaction (i.e., exercise capacity). The basic functional units of extracellular respiration are to move the oxygen: (1) into the alveoli, (2) into the blood, and (3) into the tissues (the process is reversed for carbon dioxide removal).

RESPIRATORY MECHANICS

Many tests of respiratory mechanics and volumes show correlation with postthoracotomy outcome: forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), maximal voluntary ventilation (MVV), residual volume/total lung capacity ratio (RV/TLC), and so on (see Chapter 13 on pulmonary function testing). It is useful to express these as a percent of predicted volumes corrected for age, sex, and height (e.g., FEV₁ %). Of these, the most valid single test for postthoracotomy respiratory complications is the predicted postoperative FEV₁ (ppoFEV₁ %),⁴ which is calculated as:

$$\text{ppoFEV}_1 \% = \text{preoperative FEV}_1 \% \times (1 - \% \text{ functional lung tissue removed}/100).$$

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. 53.1). Patients with a ppoFEV₁ greater than 40% are at low risk for postresection respiratory complications. The risk of major respiratory complications is increased in the subgroup with ppoFEV₁ less than 40% (although not all patients in this subgroup develop respiratory complications) and patients with ppoFEV₁ less than 30% are at high risk.

Lung 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 PaO_2 less than 60 mm Hg or PaCO_2 greater than 45 mm Hg have been used as cut-off values for pulmonary resection. Cancer resections have now been successfully done 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 correlates with the total functioning surface area of alveolar-capillary interface. The corrected DLCO can be used to calculate a postresection (predicted postoperative [ppo]) value using the same calculation as for the FEV_1 (see Fig. 53.1). A ppoDLCO less than 40% correlates with both increased respiratory and cardiac complications and is, to a large degree, independent of the FEV_1 .⁵ The DLCO, but not the FEV_1 , is negatively affected by preoperative chemotherapy and may be the most important predictor of complications in this subgroup of patients. Some authors feel a higher cutoff risk-threshold for ppoDLCO of less than 50% may be more appropriate.⁶ The National Emphysema Treatment Trial has shown that patients with a preoperative FEV_1 or DLCO less than 20% had an unacceptably high perioperative mortality rate.⁷ These can be considered as the absolute minimal values compatible with a successful outcome.

Cardiopulmonary Interaction

The final and perhaps most important assessment of respiratory function is an assessment of the cardiopulmonary interaction (evaluation of the patient's exercise capacity). Exercise capacity is commonly described in units of metabolic equivalent of task (MET). Sitting quietly requires an oxygen consumption of 3.5 mL/kg/min (1 MET). Climbing one flight of stairs is 4 METs. In a patient who is a reliable historian, the ability to climb two flights of stairs without stopping is a minimum to be considered for pulmonary resection evaluation. While there is no absolute definition

of the height of a flight of stairs, 10 feet (3 M) is a commonly used standard. Patients who cannot give a reliable history, or are limited in their ability to climb stairs because of comorbidities, will require simple and/or formal exercise testing.

The most valid simple exercise test is the maximal distance that a patient can walk in 6 minutes.⁸ The 6-minute walk test (6MWT) shows an excellent correlation with maximal oxygen consumption ($\text{VO}_{2\text{max}}$) and requires no laboratory equipment. It has been shown in COPD patients that the $\text{VO}_{2\text{max}}$ can be estimated from the 6MWT distance in meters divided by 30 (i.e., 6MWT of 450 m: estimated $\text{VO}_{2\text{max}} = 450/30 = 15 \text{ mL/kg/min}$).⁹ Other simple exercise tests include shuttle walking in which a patient walks at a fixed, and gradually increased, rate between 2 markers 10 meters apart. A distance of less 250 meters correlates with a $\text{VO}_{2\text{max}}$ of less than 10 mL/kg/min.³ Another simple test is exercise-oximetry: patients with a decrease of blood oxygen saturation (SpO_2) greater than 4% during exercise are at increased risk.

Formal laboratory exercise testing is the "gold standard" for assessment of cardiopulmonary function¹⁰ and the $\text{VO}_{2\text{max}}$ is the most useful predictor of postthoracotomy outcome. The risk of morbidity and mortality is high if the preoperative $\text{VO}_{2\text{max}}$ is less than 15 mL/kg/min, and very high if less than 10 mL/kg/min (35% predicted).¹¹ Few patients with a $\text{VO}_{2\text{max}}$ greater than 20 mL/kg/min (75% predicted) have respiratory complications. (For comparison, a $\text{VO}_{2\text{max}}$ of 85 mL/kg/min was documented for the American cyclist Lance Armstrong in 2005¹²; since then several elite rowers and cross-country skiers have exceeded this.)

After pulmonary resection, right ventricular dysfunction appears to be in proportion to the amount of functioning pulmonary vascular bed removed. The exact etiology and duration of this dysfunction remain 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 (PVR) usually seen with exertion.¹³

Ventilation Perfusion Scintigraphy

Prediction of postresection pulmonary function can be further refined by assessment of the preoperative contribution of the lung or lobe to be resected using ventilation-perfusion (V/Q) lung scanning. If the lung region to be resected is nonfunctioning or minimally functioning, the prediction of postoperative function can be modified accordingly. This is particularly useful in pneumonectomy patients and V/Q scanning should be considered for any pneumonectomy patient who has a preoperative FEV_1 and/or DLCO less than 80%. However, V/Q scanning is of limited usefulness to predict postlobectomy function.¹⁴

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

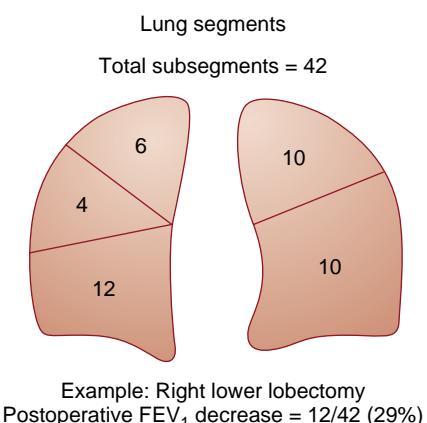


Fig. 53.1 The number of subsegments of each lobe are used to calculate the predicted postoperative (ppo) pulmonary function (e.g., after a right lower lobectomy, a patient with a preoperative FEV_1 [or DLCO] 70% of normal would be expected to have a ppo FEV_1 of 70% \times (1 – 29/100) = 50%. ppoDLCO, Predicted postoperative diffusing capacity for carbon monoxide; ppo FEV_1 , predicted postoperative forced expiratory volume. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

aspects of pulmonary function form the “three-legged stool” that is the foundation of prethoracotomy respiratory assessment (Box 53.1).

An algorithm for preoperative respiratory evaluation of the patient for pulmonary resection is presented in Fig. 53.2. The recent increased use of minimally invasive surgical techniques has had a major impact on the assessment of operability in lung cancer patients. Patients previously considered high risk for thoracotomy may not be high risk if the procedure can be done with VATS or robotic surgery.¹⁵ The threshold for increased risk in ppoFEV₁ for lobectomy appears to have shifted from less than 40% for open thoracotomy to less than 30% for VATS (Fig. 53.3).¹⁶ The same shift may also have occurred for ppoDLCO (Fig. 53.4).¹⁷

If a patient has a ppoFEV₁ greater than 40%, the trachea usually can be extubated in the operating room at the conclusion of surgery assuming the patient is alert, warm, and comfortable (“AWaC”). If the ppoFEV₁ is greater than 30% and exercise tolerance and lung parenchymal function exceed the increased-risk thresholds, then tracheal

extubation can be done in the operating room depending on the status of associated medical conditions. 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. Patients with a ppoFEV₁ of 20% to 30% and favorable predicted cardiorespiratory and parenchymal function can be considered for early tracheal extubation if thoracic epidural analgesia is used or if the resection is performed with VATS. In the increased-risk group, the presence of several associated factors and diseases should be documented during the preoperative assessment and will enter into the consideration for postoperative management (discussed later).

Concomitant Medical Conditions

CARDIAC DISEASE

Cardiac complications are the second most common cause of perioperative morbidity and mortality in the thoracic surgical population.

Ischemia

Because the majority of pulmonary resection patients have a smoking history, they already have one risk factor for coronary artery disease. Elective pulmonary resection surgery is regarded as an “intermediate-risk” procedure in terms of perioperative cardiac ischemia.¹⁸ The overall documented incidence of postthoracotomy ischemia is 5% and peaks on days 2 to 3 postoperatively. Beyond the standard history, physical, and electrocardiogram, routine screening testing for cardiac disease does not appear to be cost-effective for

BOX 53.1 The Three-Legged Stool of Prethoracotomy Respiratory Assessment

Respiratory mechanical function. Most valid test: ppoFEV₁. Threshold for increased risk: <30%–40% (see text)

Lung parenchymal function. Most valid test: ppoDLCO. Threshold for increased risk: <30%–40% (see text)

Cardiopulmonary interaction. Most valid test: Maximal oxygen consumption. Threshold for increased risk: <15 mL/kg/min

ppoDLCO, Predicted postoperative diffusing capacity for carbon monoxide; ppoFEV₁, predicted postoperative forced expiratory volume.

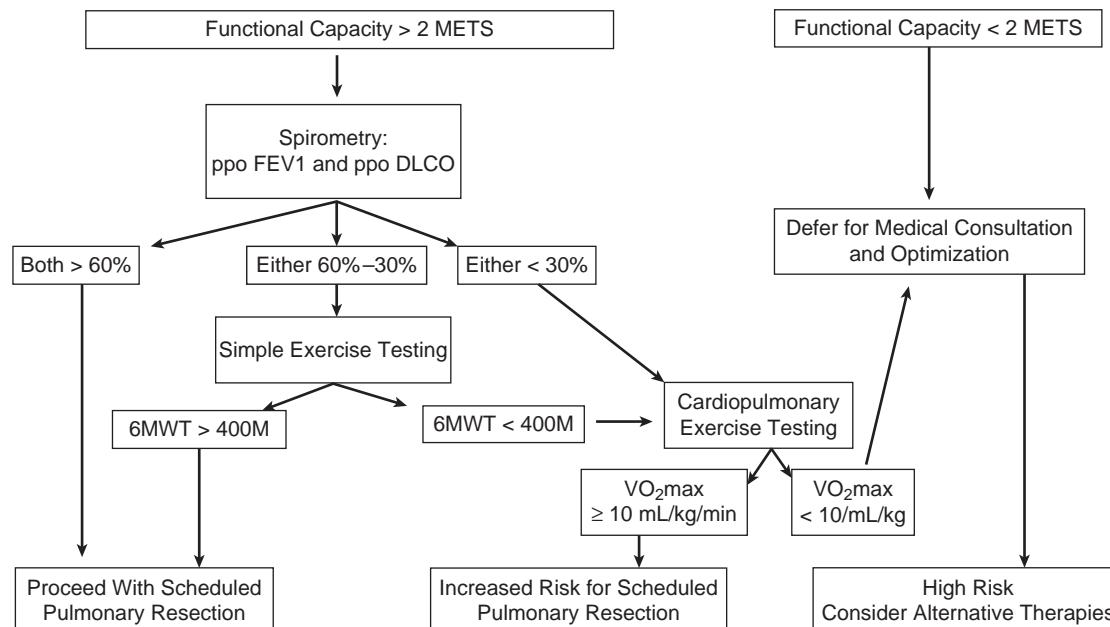


Fig. 53.2 A flow-diagram for preoperative respiratory investigation of a patient for pulmonary resection surgery. MET, Metabolic equivalent of task; ppoDLCO, predicted postoperative diffusing capacity for carbon monoxide; ppoFEV₁, predicted postoperative forced expiratory volume in 1 second; 6MWT, = 6-minute walk test distance in meters. (Based on data from Brunelli A, Kim A, et al. Physiological evaluation of the patient with lung cancer being considered for resectional surgery. *Chest*. 2013;143:e166s–190s; and Licker M, Triponez F, Diaper J, et al. Preoperative evaluation of lung cancer patients. *Curr Anesthesiol Rep*. 2014;4:124–134.)

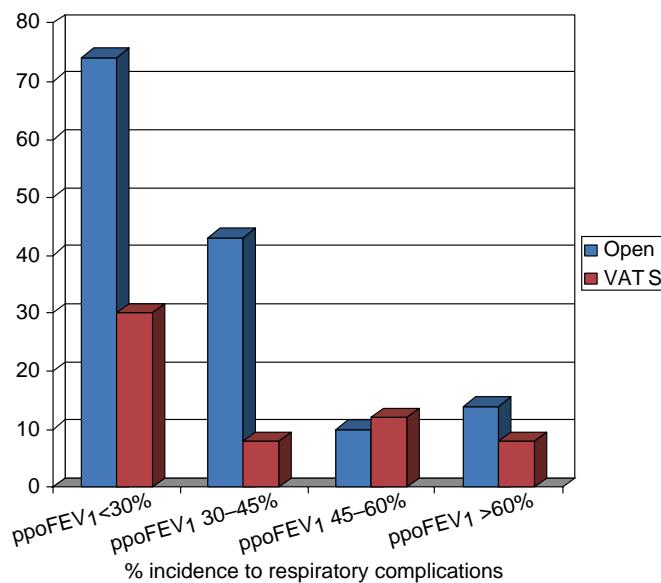


Fig. 53.3 A comparison of the incidence of postoperative respiratory complications after open thoracotomy versus VATS lobectomies for lung cancer. FEV₁, forced expiratory volume in one second; ppo, Predicted postoperative value; VATS, video-assisted thoracoscopic surgery. This was a nonrandomized retrospective study. It appears that the threshold for increased risk may have decreased from <40% ppoFEV₁ in the open group to <30% in the VATS group. (Based on data from Berry M, et al. *Ann Thorac Surg*. 2010;89:1044-1052.)

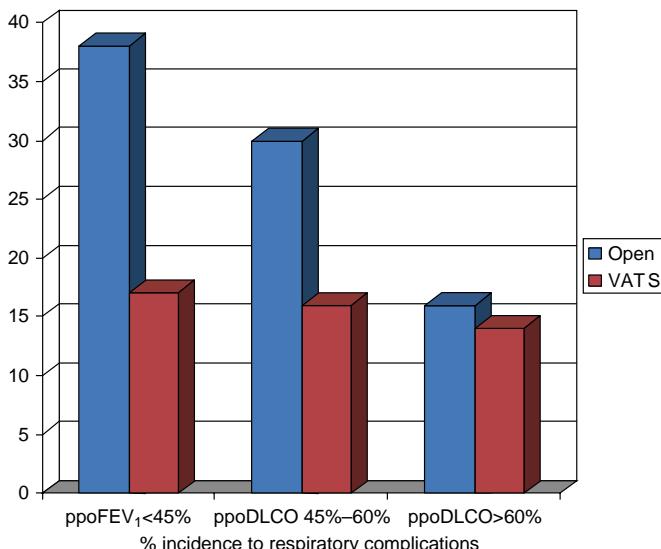


Fig. 53.4 A comparison of the incidence of postoperative respiratory complications after open thoracotomy versus VATS lobectomies for lung cancer. DLCO, diffusing capacity for carbon monoxide; ppo, Predicted postoperative value; VATS, video-assisted thoracoscopic surgery. It appears there is a threshold for increased risk in open procedures with less than 60% ppoDLCO. A threshold for VATS procedures could not be clearly identified, however there were very few patients with a ppoDLCO <40% in this study. (Based on data from Berry M, et al. *Ann Thorac Surg*. 2010;89:1044-1052.)

all prethoracotomy patients. Noninvasive testing is indicated in patients with major (i.e., unstable ischemia, recent infarction, severe valvular disease, significant arrhythmia) or intermediate (i.e., stable angina, remote infarction, previous congestive failure, diabetes) clinical predictors of myocardial risk. Therapeutic options to be considered in patients

with significant coronary artery disease are optimization of medical therapy, coronary angioplasty, or coronary artery bypass, either before or at the time of lung resection. Timing of lung resection surgery after a myocardial infarction is always a difficult decision to make. Limiting the delay to 4 to 6 weeks in a medically stable and fully investigated and optimized patient seems acceptable after myocardial infarction. The appropriate delay after coronary stenting is conventionally 4 to 6 weeks after bare metal stents and 6 months after drug-eluting stents.^{19,20} Surgery should be delayed until it is safe to temporarily discontinue major antiplatelet drugs (except aspirin).²⁰ Preoperative investigation of the patient with coronary artery disease for pulmonary resection should follow the most recent guidelines of the American College of Cardiology (see Chapter 31).²¹

Arrhythmia

Dysrhythmias are a common complication of pulmonary resection surgery and the incidence is 30% to 50% of patients in the first week postoperatively, when Holter monitoring is used.²² Of these arrhythmias, 60% to 70% are atrial fibrillation. Several factors correlate with an increased incidence of arrhythmias, including extent of lung resection (pneumonectomy, 60%; vs. lobectomy, 40%; vs. nonresection thoracotomy, 30%), intrapericardial dissection, intraoperative blood loss, and age of the patient. Extrapleural pneumonectomy patients are a particularly high-risk group.²³

Two factors in the early postthoracotomy period interact to produce atrial arrhythmias: 1. increased flow resistance through the pulmonary vascular bed because of permanent (lung resection) or transient (atelectasis, hypoxemia) causes, with attendant strain on the right side of the heart; and 2. increased sympathetic stimuli and oxygen requirements, which are maximal on the second postoperative day as patients become more mobile.

In some patients undergoing a pneumonectomy, the right heart may not be able to increase its output adequately to meet the usual postoperative stress. Trans-thoracic 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 postthoracotomy supraventricular tachyarrhythmias.²⁴ Preoperative exercise testing, which assesses the cardiopulmonary interaction, can predict postthoracotomy arrhythmias. Patients with COPD are more resistant to pharmacologic-induced heart rate control when they develop postthoracotomy atrial fibrillation and often require multiple drugs.²⁵

Guidelines for the prevention of atrial fibrillation after thoracic surgery written by the American Association of Thoracic Surgeons are presented in Table 53.1.²⁶ At present, diltiazem is the most useful drug for postthoracotomy arrhythmia prophylaxis.¹⁹ It seems that atrial arrhythmias are a sign of the dysfunctional right heart and preventing the complication does not solve the underlying problem. β -Adrenergic blockers may be the most effective drug to prevent arrhythmias, but there are concerns about their routine use in patients with reactive airways diseases.²⁷

TABLE 53.1 Recommendations for Prevention of Postoperative Atrial Fibrillation (AF) in Thoracic Surgery

All Patients	High Risk for AF
	Includes: Anterior mediastinal mass, lobectomy, pneumonectomy, and esophagectomy
Continue β -blockers if taken preoperatively	Diltiazem, if preserved cardiac function and not taking β -blockers
Magnesium if serum level is low or suspected total body stores depleted	Consider amiodarone
	Consider statins

Based on 2014 AATS Guidelines. Frendl G, Sodickson A, et al. *J Thorac Cardiovasc Surg*. 2014;148:772–791.

BOX 53.2 Modified Classification of Pulmonary Hypertension for Anesthesia

Left Heart Disease	Lung Disease
Systolic dysfunction	Pulmonary vascular disease
Diastolic dysfunction	Chronic lung diseases, hypoxemia, sleep apnea
Mitral valvular disease: stenosis, regurgitation	Thromboembolic pulmonary hypertension
Congenital cardiac disease	Miscellaneous: Autoimmune, metabolic, etc.

Congestive Heart Failure

During one-lung ventilation (OLV) for thoracotomy or thoracoscopy there is an obligate 20% to 30% shunt through the nonventilated lung. If the baseline cardiac output is decreased, the fall in mixed venous oxygen saturation (SvO_2) will lead to an exaggerated fall in arterial oxygen saturation. Patients with a history of congestive heart failure and/or cardiomyopathy may tolerate OLV poorly. They will need monitoring of venous saturation and inotropes to support cardiac output.

Pulmonary Hypertension

Patients with degrees of pulmonary hypertension (mean pulmonary arterial pressure [PAP] > 25 mmHg by catheterization or systolic PAP > 35)²⁸ may present for a variety of noncardiac thoracic surgical procedures including pulmonary resections for malignant or benign lesions, esophageal surgery, or vascular surgery.²⁹ Compared to patients with normal pulmonary pressures, patients with pulmonary hypertension are particularly at increased risk of respiratory complications and the need for prolonged intubation after noncardiac surgery.³⁰ There are five different major diagnostic groups in the classification of pulmonary hypertension, with multiple subgroups of each group.³¹ However, for the anesthesiologist, there are two main types of pulmonary hypertension: pulmonary hypertension due to left heart disease and pulmonary hypertension due to lung disease (Box 53.2). Most of the anesthesia literature has focused on patients with underlying cardiac disease.³² However, patients who present for noncardiac surgery are more likely to have pulmonary hypertension secondary to lung disease.³³ The prevalence of pulmonary hypertension in severe chronic lung disease ranges from 40% to 50%.³⁴

The myocardium of the right ventricle is normally perfused throughout the cardiac cycle. The increased right ventricular transmural and intracavitory pressures associated with pulmonary hypertension may restrict perfusion of the right coronary artery during systole, especially as PAPs approach systemic levels. Avoiding hypotension is key to managing these patients. In practice, this can be a challenge to achieve because anesthetics are commonly associated with a decrease in systemic vascular resistance (SVR) (e.g., propofol and inhalation anesthetics) and a variable effect on PVR. Ketamine or etomidate are useful anesthetic induction drugs in pulmonary hypertension due to lung disease.³⁵ Inotropes and inodilators such as dobutamine and milrinone may improve hemodynamics in patients with pulmonary hypertension secondary to left heart disease. However, they can decrease systemic vascular tone and tachycardia, and can cause a deterioration in the hemodynamics of patients with pulmonary hypertension due to lung disease. To maintain a systemic arterial blood pressure that is greater than the pulmonary pressure, vasopressors such as phenylephrine or norepinephrine are commonly used.³⁶ Vasopressin is also useful to maintain systemic pressures. Vasopressin appears to significantly increase systolic blood pressure without affecting PAP in patients with pulmonary hypertension (Fig. 53.5).^{37,38} In patients with severe pulmonary hypertension, selective inhaled pulmonary vasodilators including nitric oxide (NO; 10–40 ppm)³⁹ or nebulized prostaglandins (prostacyclin 50 ng/kg/min) (Fig. 53.6)⁴⁰ should be considered (Box 53.3).

At present, the basis of intraoperative monitoring for a patient with pulmonary hypertension having noncardiac thoracic surgery remains the pulmonary artery catheter. However, pulmonary artery data alone can be misleading in these patients. Rising pulmonary artery pressures are almost always a bad sign. Falling pulmonary artery pressures may be a good sign, indicating pulmonary vasodilation, or may be a very bad sign indicating impending right ventricular decompensation. Thus pulmonary artery pressure data need to be followed in concert with cardiac output or mixed venous saturation data. Transesophageal echocardiography (TEE) is also helpful to monitor right heart function during thoracic surgery. Advances in echocardiography technology may make continuous objective monitoring of right ventricle function more possible in the near future.⁴¹

Although there have been multiple case reports of the successful use of lumbar epidural analgesia and anesthesia in obstetric patients with pulmonary hypertension,⁴² there are very few reports of the use of thoracic epidural analgesia in pulmonary hypertension. Patients with pulmonary hypertension due to lung disease seem to be extremely dependent on tonic cardiac sympathetic innervation for normal hemodynamic stability. Animal studies suggest that the hemodynamic response to an increase in right ventricular afterload is very different with thoracic versus lumbar epidurals. In one study, right ventricle contractility increased as afterload increased in animals with lumbar epidural local anesthetic blockade, similar to the response in animals without neuraxial block. The cardiac sympathectomy of thoracic epidural blockade abolished this increase in contractility (Fig. 53.7).⁴³ Because of the increased risk of postoperative respiratory complications in these patients,

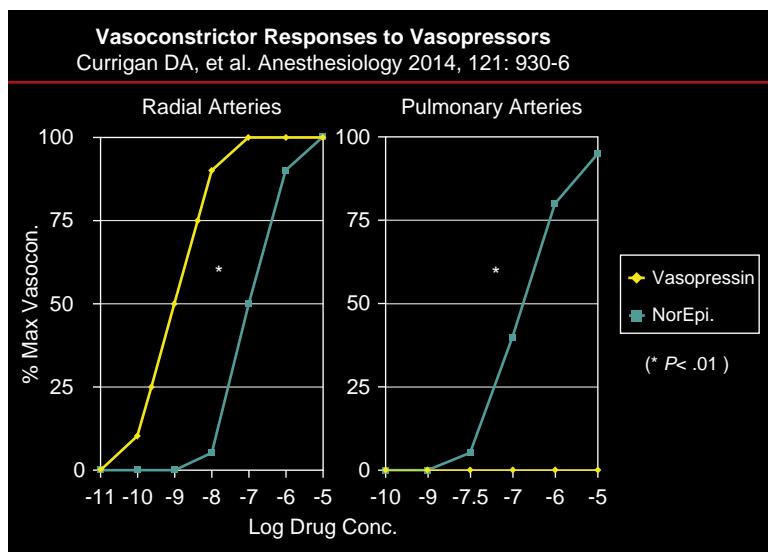


Fig. 53.5 In vitro maximal vasoconstriction (Max Vasocon.) dose-response curves of human radial arteries (left) and pulmonary arteries (right) to vasopressin and norepinephrine (NorEpi). All vasoconstrictors studied (including phenylephrine and metaraminol) showed similar dose-response patterns in both types of arteries except vasopressin, which showed no constriction of pulmonary arteries. (Based on data from: Curriган DA, Hughes RJA, Wright CE, et al. Vasoconstrictor responses to vasopressor agents in human pulmonary and radial arteries. *Anesthesiology*. 2014;121:930–936.)

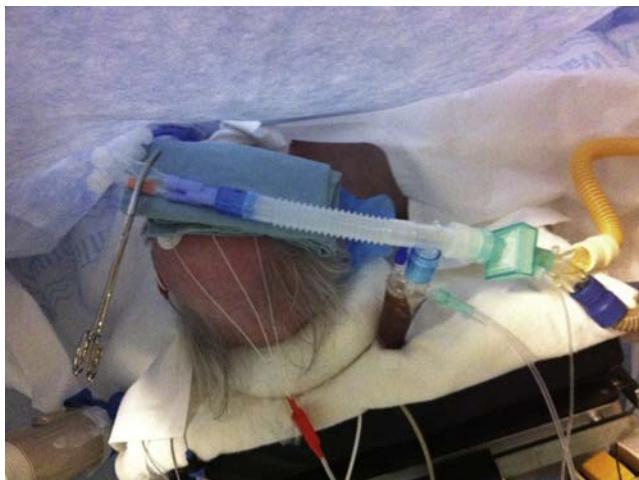


Fig. 53.6 Prostacyclin can be delivered continuously into a standard anesthetic circuit and the dose titrated as needed. In the photograph prostacyclin is delivered by nebulization to the ventilated lung via a double-lumen tube during thoracic surgery and one-lung ventilation in a patient with pulmonary hypertension.

BOX 53.3 Management Principles for Pulmonary Hypertension Secondary to Lung Disease

1. Avoid hypotensive and vasodilating anesthetic agents whenever possible
2. Ketamine does not exacerbate pulmonary hypertension
3. Support mean systolic pressure with vasopressors: norepinephrine, phenylephrine, vasopressin
4. Use inhaled pulmonary vasodilators (nitric oxide, prostacyclin) in preference to intravenous vasodilators when necessary
5. Use thoracic epidural local anesthetics cautiously and with inotropes when necessary
6. Monitor cardiac output

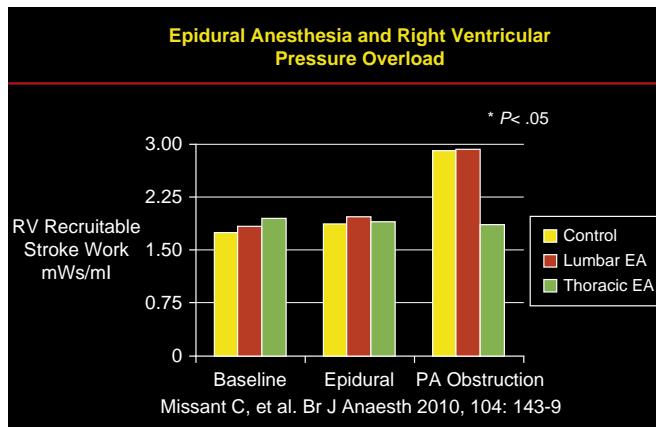


Fig. 53.7 Right ventricular (RV) recruitable stroke work, a measure of RV contractility, measured in three groups of anesthetized pigs: Control, no epidural group; Lumbar EA, lumbar epidural group; Thoracic EA, thoracic epidural group. Epidural bupivacaine injection had no effect on RV function in any of the study groups. Subsequent inflation of a balloon in the main pulmonary artery (PA Obstruction), increased RV afterload and resulted in a compensatory increase in RV contractility in the Control and Lumbar EA groups but not in the Thoracic EA group. (Based on data from Missant C, Claus P, Rex S, Wouters PF. Differential effects of lumbar and thoracic epidural anaesthesia on the haemodynamic response to acute right ventricular pressure overload. *Br J Anaesth*. 2009;104:143–149.)

the use of postoperative thoracic epidural analgesia is often desirable. However, these patients often require a low-dose infusion of inotropes or vasopressors during thoracic epidural local analgesia, which may necessitate continued central venous catheterization and intensive care unit admission. Paravertebral analgesia has been associated with better postthoracotomy hemodynamic stability versus thoracic epidural analgesia in patients with normal cardiac function⁴⁴ but this has not been specifically studied in pulmonary hypertensive patients.

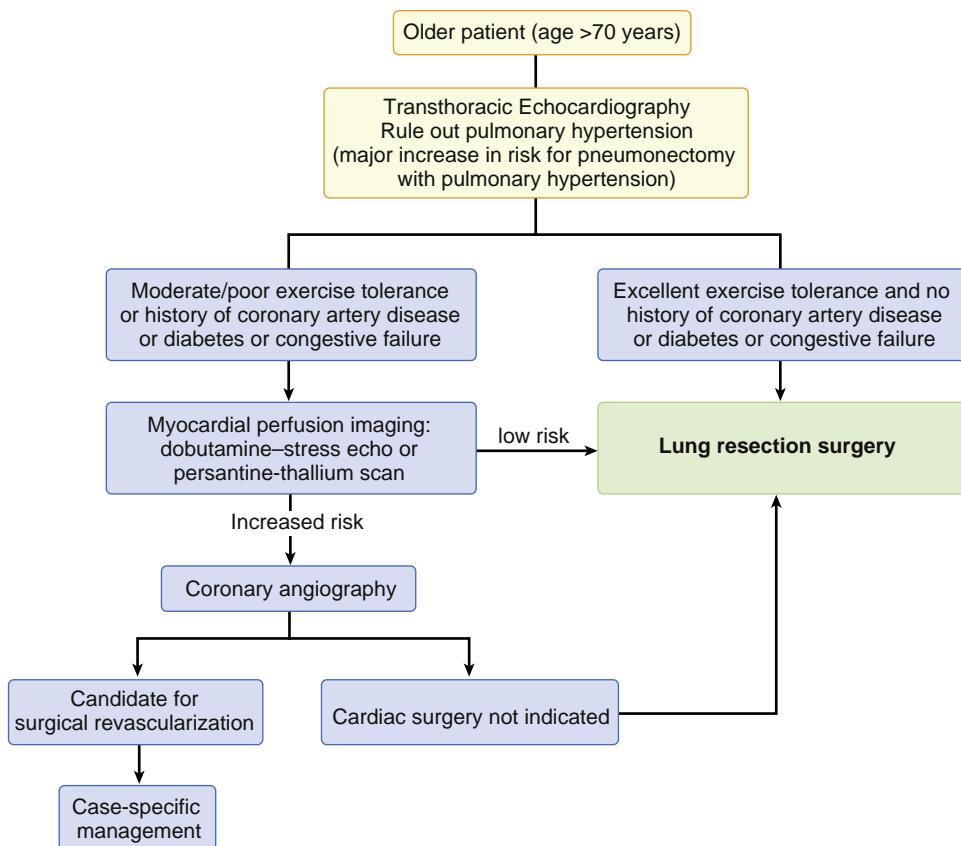


Fig. 53.8 Algorithm for the preoperative cardiac assessment of older patients for thoracic (noncardiac) surgery.

AGE

There is no maximum age that is a cutoff for pulmonary resection.⁴ The operative mortality in a group of patients 80 to 92 years of age was 3%, a very respectable figure, in one series.⁴⁵ 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 older patients, 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 elderly for thoracic surgery is presented in Fig. 53.8. Although the mortality resulting from lobectomy among the older patients is acceptable, the mortality from pneumonectomy, particularly right pneumonectomy, is excessive.⁴⁶ Quality of life after pneumonectomy is significantly worse than after lesser pulmonary resections.⁴⁷ For these reasons, lung-sparing pulmonary resections are performed whenever possible. As a proportion of all lung cancer resections, pneumonectomy has decreased to approximately one third of its share of 15 years ago.⁴⁸ Exercise tolerance seems to be the primary determinant of outcome in older patients. Older patients should have, as a minimum cardiac investigation, a transthoracic echocardiogram to rule out pulmonary hypertension.

RENAL DYSFUNCTION

Renal dysfunction following pulmonary resection surgery was previously associated with a high mortality. Golledge

and Goldstraw⁴⁹ reported a perioperative mortality of 19% (6/31) in patients in whom a significant elevation of serum creatinine developed in the postthoracotomy period, compared with 0% (0/99) in those who did not show any renal dysfunction. More recently, postthoracotomy renal dysfunction has not been found to be associated with increased mortality.⁵⁰ Predictive factors for renal dysfunction include preoperative hypertension, angiotensin II receptor blockers, use of hydroxyethyl starch, and open thoracotomies.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The most common concurrent illness in the thoracic surgical population is 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.⁵¹ Assessment of the severity of COPD is made on the basis of the FEV₁% of predicted values. The American Thoracic Society categorizes stage I as greater than 50% predicted, stage II as 35% to 50%, and stage III as less than 35%. Stage I patients should not have significant dyspnea, hypoxemia, or hypercarbia, and other causes should be considered if these are present.

Respiratory Drive

Many patients with stage II or III COPD have an elevated PaCO₂ at rest. It is not possible to differentiate these "CO₂-retainers" from nonretainers on the basis of history, physical examination, or spirometric pulmonary function

testing.⁵² CO₂ retention is related more to an inability to maintain the increased work of respiration (W_{resp}) required to keep the PaCO₂ normal in patients with mechanically inefficient pulmonary function and not primarily resulting from an alteration of respiratory control mechanisms. It was previously thought that chronically hypoxicemic/hypercapnic patients relied on a hypoxic stimulus for ventilatory drive and became insensitive to PaCO₂. This explained the clinical observation that COPD patients in incipient respiratory failure could be put into a hypercapnic coma by the administration of a high concentration of oxygen (fraction of inspired oxygen [FiO₂]). In actuality, only a minor fraction of the increase in PaCO₂ in such patients is caused by a diminished respiratory drive, because minute ventilation is basically unchanged.⁵³ The PaCO₂ rises because a high FiO₂ causes a relative decrease in alveolar ventilation 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 decreased⁵⁴ and also as a result of the Haldane effect.⁵⁵ 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 PaCO₂ should be anticipated and monitored. To identify these patients preoperatively, all stage II and III COPD patients need an arterial blood gas analysis.

Nocturnal Hypoxemia

COPD patients desaturate more frequently and severely than normal patients during sleep.⁵⁶ This is due to the rapid/shallow breathing pattern that occurs in all patients during REM sleep. In COPD patients breathing air, this causes a significant increase in the respiratory dead space/tidal volume (V_D/V_T) ratio and a fall in alveolar oxygen tension (PAO₂) and PaO₂. This is not the sleep-apnea-hypoventilation syndrome (SAHS). There is no increased incidence of SAHS in COPD.

Right Ventricular Dysfunction

Right ventricular dysfunction occurs in as many as 50% of COPD patients. The dysfunctional right ventricle is poorly tolerant of sudden increases in afterload⁵⁷ such as the change from spontaneous to controlled ventilation.⁵⁸

Right ventricular function becomes critical in maintaining cardiac output as the pulmonary artery pressure rises. The RV ejection fraction does not increase with exercise in COPD patients as it does in normal patients. Chronic recurrent hypoxemia is the cause of the RV dysfunction and the subsequent progression to cor pulmonale. Patients who have episodic hypoxemia in spite of normal lungs (e.g., central alveolar hypoventilation, SAHS)⁵⁹ develop the same secondary cardiac problems as COPD patients. The only therapy that improves long-term survival and decreases right-sided heart strain in COPD is administration of increasing concentrations of oxygen. COPD patients who have a resting PaO₂ less than 55 mm Hg, as well as those who have decreases to less than 44 mm Hg with exercise, should receive supplemental oxygen at home. The goal of supplemental oxygen is to maintain a PaO₂ 60 to 65 mm Hg. Compared with patients with chronic bronchitis, emphysematous COPD patients tend to have a decreased cardiac output and mixed venous oxygen tension while maintaining lower pulmonary artery pressures.

Bullae

Many patients with moderate or severe COPD will develop cystic air spaces in the lung parenchyma known as bullae. These bullae will often be asymptomatic unless they occupy more than 50% of the hemithorax, in which case the patient will present with findings of restrictive respiratory disease in addition to their obstructive disease. A bulla is a localized area of loss of structural support tissue in the lung with elastic recoil of surrounding parenchyma (Fig. 53.9). The pressure in a bulla is actually the mean pressure in the surrounding alveoli averaged over the respiratory cycle. This means that during normal spontaneous ventilation the intrabulla pressure is actually slightly negative in comparison to the surrounding parenchyma.⁶⁰ However, whenever positive-pressure ventilation is used the pressure in a bulla will become positive in relation to the adjacent lung tissue and the bulla will expand with the attendant risk of rupture, tension pneumothorax, and bronchopleural fistula. Positive-pressure ventilation can be used safely in patients with bullae provided the airway pressures are kept low and there is adequate expertise and equipment immediately available to insert a chest drain and obtain lung isolation if necessary. Management of patients for bullectomy is discussed later.

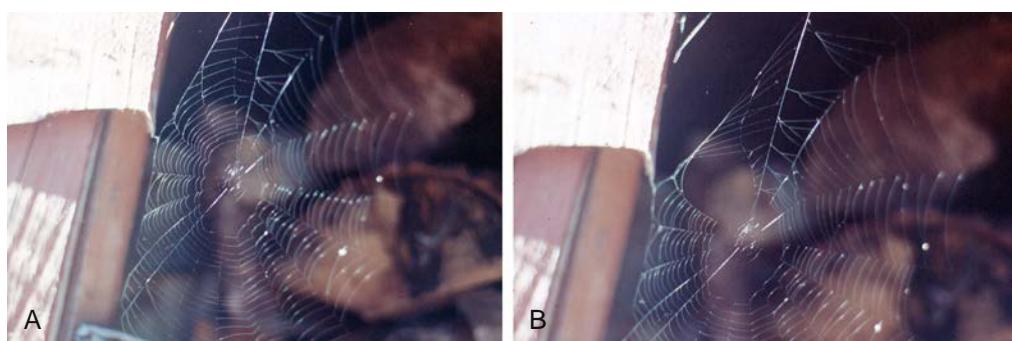


Fig. 53.9 (A) A spider's web as a lung model to demonstrate the pathophysiology of bullae. (B) Breaking one septum of the spider's web causes a bulla to appear as elastic recoil pulls the web away from the area where structural support has been lost. Although the cells surrounding the bulla appear compressed, this is only because of redistribution of elastic forces. It is not positive pressure inside the bulla that causes this appearance of surrounding compression. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

Flow limitation

Severe COPD patients are often “flow-limited” even during tidal volume expiration at rest.⁶¹ Flow limitation is present in normal patients only during a forced expiratory maneuver. Flow limitation occurs when an equal pressure point (EPP) develops in the intrathoracic airways during expiration. During quiet expiration in the normal patient the pressure in the lumen of the airways always exceeds the intrapleural pressure because of the upstream elastic recoil pressure which is transmitted from the alveoli. The effect of this elastic recoil pressure diminishes as air flows downstream in the airway. With a forced expiration the intrapleural pressure may equal the intraluminal pressure at a certain point, the EPP, which then limits the expiratory flow. Then, any increase in expiratory effort will not produce an increase in flow at that given lung volume.⁶²

Flow limitation occurs particularly in emphysematous patients, who primarily have a problem with loss of lung elastic recoil and have marked dyspnea on exertion. Flow limitation causes dyspnea because of stimulation of mechanoreceptors in the muscles of respiration, thoracic cage, and in the airway distal to the EPP. Any increase in the work of respiration will lead to increased dyspnea. This variable mechanical compression of airways by over-inflated alveoli is the primary cause of the airflow obstruction in emphysema.

Severely flow-limited patients are at risk for hemodynamic collapse with the application of positive-pressure ventilation due to dynamic hyperinflation of the lungs. Even the modest positive airway pressures associated with manual ventilation with a bag/mask at induction can lead to hypotension since these patients have no increased resistance to inspiration but a marked obstruction of expiration. In some of these patients this has contributed to the “Lazarus” syndrome in which patients have recovered from a cardiac arrest only after resuscitation and positive-pressure ventilation were discontinued.⁶³

Auto-Positive End-Expiratory Pressure

Patients with severe COPD often breathe in a pattern that interrupts expiration before the alveolar pressure has fallen to atmospheric pressure. This incomplete expiration is due to a combination of factors which include flow limitation, increased work of respiration, and increased airway resistance. This interruption leads to an elevation of the end-expiratory lung volume above the FRC. This positive end-expiratory pressure (PEEP) in the alveoli at rest has been termed auto-PEEP or intrinsic-PEEP. During spontaneous respiration the intrapleural pressure will have to be decreased to a level which counteracts auto-PEEP before inspiratory flow can begin. Thus COPD patients can have an increased inspiratory load added to their already increased expiratory load.

Auto-PEEP becomes even more important during mechanical ventilation. It is directly proportional to tidal volume and inversely proportional to expiratory time. The presence of auto-PEEP is not detected by the manometer of standard anesthesia ventilators. It can be measured by end-expiratory flow interruption, a feature available on most intensive care ventilators. Auto-PEEP has been found to develop in most COPD patients during one-lung anesthesia.⁶⁴

PREOPERATIVE THERAPY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

There are four treatable complications of COPD that must be actively sought and therapy begun at the time of the initial prethoracotomy assessment. These are: atelectasis, bronchospasm, respiratory tract infections, and pulmonary edema (Table 53.2). Atelectasis impairs local lung lymphocyte and macrophage function predisposing to infection. Pulmonary edema can be very difficult to diagnose by auscultation in the presence of COPD and may present very abnormal radiological distributions (e.g., unilateral, upper lobes). Bronchial hyperreactivity may be a symptom of congestive failure or may represent an exacerbation of reversible airways obstruction. All COPD patients should receive maximal bronchodilator therapy as guided by their symptoms. Only 20% to 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.

PHYSIOTHERAPY

Patients with COPD have fewer postoperative pulmonary complications when a perioperative program of intensive chest physiotherapy is initiated preoperatively.⁶⁵ Among the different modalities available (cough and deep breathing, incentive spirometry, PEEP, continuous positive airway pressure [CPAP]), there is no clearly proven superior method. Family members or nonphysiotherapy 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 1 month. Among COPD patients, those with excessive sputum benefit the most from chest physiotherapy.

A comprehensive program of pulmonary rehabilitation involving physiotherapy, exercise, nutrition, and education can improve functional capacity for patients with severe COPD.⁶⁶ These programs are usually of several months duration and are generally not an option in resections for malignancy although for nonmalignant resections in severe COPD patients, rehabilitation should be considered. The benefits of short duration rehabilitation programs prior to malignancy resection have not been fully assessed.

Smoking: Pulmonary complications are decreased in thoracic surgical patients who cease smoking for more

TABLE 53.2 Concurrent Problems That Should Be Treated Prior to Anesthesia in Chronic Obstructive Pulmonary Disease Patients

Problem	Method of Diagnosis
Bronchospasm	Auscultation
Atelectasis	Chest radiograph
Infection	History, sputum analysis
Pulmonary edema	Auscultation, chest radiograph

than 4 weeks before surgery.⁶⁷ Carboxyhemoglobin concentrations decrease if smoking is stopped more than 12 hours.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. There is no rebound increase in pulmonary complications if patients stop for shorter (<8 week) periods before surgery.⁶⁹ Intensive smoking-cessation interventions are the most successful.⁷⁰

PRIMARY THORACIC TUMORS

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. There are over 200,000 new cases of lung cancer diagnosed per year in North America and more than 1.2 million in the world. 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 to 1970.⁷¹

Lung cancer is broadly divided into small-cell lung cancer (SCLC) and non–small-cell lung cancer (NSCLC), with about 75% to 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 localized fibrous tumors of pleura (previously referred to as benign mesotheliomas) and malignant pleural mesothelioma (MPM). Asbestos exposure is implicated 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 to 50 years.

Tobacco smoke is responsible for approximately 90% of all lung cancers and the epidemiology of lung cancer follows the epidemiology of cigarette smoking with approximately a 3-decade lag time.⁷² 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. Assuming current mortality patterns continue, cancer will pass heart disease as the leading cause of death in North America in this decade.

Non-Small-Cell Lung Cancer

This pathologically heterogeneous group of tumors includes squamous cell, adenocarcinoma, and large-cell carcinoma. Overall 5-year survival with surgery approaches 40%. This seemingly low figure must be viewed in the light of an estimated 5-year survival without surgery of less than 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

TABLE 53.3 Anesthetic Considerations for Different Types of Lung Cancer

Type	Considerations
Squamous cell	Central lesions (predominantly) Often with endobronchial tumor Mass effects: obstruction, cavitation Hypercalcemia
Adenocarcinoma	Peripheral lesions Extrapulmonary invasion common Most Pancoast tumors Growth hormone, corticotropin Hypertrophic osteoarthropathy
Large Cell	Large, cavitating peripheral tumors Similar to adenocarcinoma
Small Cell	Central lesions (predominantly) Surgery usually not indicated Paraneoplastic syndromes Lambert-Eaton syndrome Fast growth rate Early metastases
Carcinoid	Proximal, endobronchial Bronchial obstruction with distal pneumonia Highly vascular Benign (predominantly) No association with smoking 5 year survival >90% Carcinoid syndrome (rarely)

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 53.3.

Squamous Cell Carcinoma

This subgroup of NSCLC is 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 may be associated with this cell type due to elaboration of a parathyroid-like factor and not due to bone metastases.

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, bones, liver, and adrenals. They often invade extrapulmonary structures, including chest wall, diaphragm, and pericardium. Almost all Pancoast tumors are adenocarcinomas. A variety of paraneoplastic metabolic factors can be secreted by adenocarcinomas such as growth hormone and corticotropin. Hypertrophic pulmonary osteoarthropathy (HPOE) is particularly associated with adenocarcinoma.

Bronchioloalveolar carcinoma 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. Because of its low potential to spread outside of the lungs, multifocal bronchioloalveolar carcinoma can be treated by lung transplantation.⁷³

Large-Cell Undifferentiated Carcinoma

This is the least common of the NSCLCs. It tends to present as a large, often cavitating peripheral tumor. The 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. Surgery is only very rarely indicated. The staging system differs from NSCLC and is divided simply into limited stage and extensive stage. 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 aggressive 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.

SCLC is known to cause a variety of paraneoplastic syndromes due to the production of peptide hormones and antibodies. The most common of these is hyponatremia, usually as a result of an inappropriate production of antidiuretic hormone (syndrome of inappropriate antidiuretic hormone secretion). Cushing syndrome and hypercortisolism through ectopic production of adrenocorticotrophic hormone are also commonly seen.

A rare neurologic paraneoplastic syndrome associated with small-cell lung tumors is the Lambert-Eaton (also called Eaton-Lambert) 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 showing increasing amplitude of unusual action potentials with high-frequency stimulation. Similar to true myasthenia gravis patients, myasthenic syndrome patients are extremely sensitive to nondepolarizing muscle relaxants. However, they respond poorly to anticholinesterase reversal agents.⁷⁴ It is important to realize that there may be subclinical involvement of the diaphragm and muscles of respiration. Thoracic epidural analgesia has been used following thoracotomy in these patients without complication. These patients' neuromuscular function may improve following resection of the lung cancer.

Carcinoid Tumors

These are part of a continuum of neuroendocrine tumors that form a spectrum of diseases from SCLC as the most malignant to typical carcinoid as the most benign. Five-year survival following resection for typical carcinoid exceeds 90%. Systemic metastasis is rare, as is the carcinoid syndrome, which is caused by the ectopic synthesis of vasoactive mediators, and is usually seen with carcinoid tumors of gut origin that have metastasized to the liver.

Atypical carcinoid tumors are more aggressive and may metastasize. Carcinoid tumors can precipitate an intraoperative hemodynamic crisis or coronary artery spasm even during bronchoscopic resection.⁷⁵ 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.⁷⁶

Pleural Tumors

Localized fibrous tumors of pleura are usually large, space occupying masses that are attached to visceral or parietal pleura. They can be either benign or malignant.

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 years. The tumor initially proliferates within the visceral and parietal pleura, typically forming a bloody effusion. Most patients present with shortness of breath or dyspnea on exertion from this pleural effusion. Thoracentesis often relieves the symptoms but rarely provides a diagnosis. Pleural biopsy by VATS is most efficient to secure a diagnosis and talc pleurodesis is performed during the same anesthetic to treat the effusion.

MPMs respond poorly to therapy and the median survival is less than 1 year. In patients with 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 intraoperative and postoperative.⁷⁷ Blood loss from the denuded chest wall or major vascular structures is always a risk. Complications related to resection of the diaphragm and pericardium are additional risks to that of pneumonectomy.

ASSESSMENT OF THE PATIENT WITH LUNG CANCER

At the time of initial assessment, cancer patients should be assessed for the “4 Ms” associated with malignancy (Box 53.4): mass effects, metabolic abnormalities, metastases, and medications. The prior use of medications that can exacerbate oxygen-induced pulmonary toxicity, such as bleomycin, should be considered.⁷⁸ Bleomycin is not used to treat primary lung cancers, but patients presenting for excision of lung metastases from germ-cell tumors 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 management is to use the lowest FiO_2 consistent with patient safety and closely monitor oximetry in any patient who has received bleomycin. We have seen lung cancer patients who received preoperative chemotherapy with cisplatin and then developed an elevation of serum creatinine when they received NSAIDs postoperatively. For this

BOX 53.4 Anesthetic Considerations in Lung Cancer Patients (the “4 Ms”)

1. Mass effects: Obstructive pneumonia, lung abscess, SVC syndrome, tracheobronchial distortion, Pancoast syndrome, recurrent laryngeal nerve or phrenic nerve paresis, chest wall or mediastinal extension
2. Metabolic effects: Lambert-Eaton syndrome, hypercalcemia, hyponatremia, Cushing syndrome
3. Metastases: Particularly to brain, bone, liver, and adrenal
4. Medications: Chemotherapy agents, pulmonary toxicity (bleomycin, mitomycin), cardiac toxicity (doxorubicin), renal toxicity (cisplatin)

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 discussion of postoperative analgesia is presented at the end of this chapter. 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. These include the addition of neuraxial blockade, paravertebral blocks, and antiinflammatories to narcotic-based analgesia. However, only epidural techniques have been shown to consistently have the capability to decrease postthoracotomy respiratory complications in high-risk patients.² Continuous paravertebral blockade may offer comparable analgesia with a lower rate of block failure and fewer side effects.⁷⁹

At the time of initial preanesthetic assessment, the risks and benefits of the various forms of postthoracotomy 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. If the patient is to receive prophylactic anticoagulants and the use of epidural analgesia has been elected, appropriate timing of anticoagulant administration and neuraxial catheter placement need to be arranged. American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines suggest an interval of 2 to 4 hours before or 1 hour after catheter placement for prophylactic heparin administration.⁸⁰ Low-molecular-weight heparin (LMWH) recommendations and precautions are: (1) a minimal interval of 12 hours after low-dose LMWH and (2) 24 hours after higher-dose LMWH before catheter placement.

PREMEDICATION

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 antisialagogue (e.g., glycopyrrolate) is useful to facilitate fiberoptic bronchoscopy for positioning of a double-lumen endobronchial tube (DLT) or bronchial blocker. To avoid an intramuscular injection, this can be given orally or intravenously immediately after placement of the intravenous

BOX 53.5 Initial Preanesthetic Assessment for Thoracic Surgery

1. All patients: assess functional capacity, spirometry, discuss postoperative analgesia, discontinue smoking
2. Patients with ppoFEV_1 or $\text{DLCO} < 60\%$: exercise test
3. Cancer patients: consider the 4 Ms: mass effects, metabolic effects, metastases, medications
4. COPD patients: arterial blood gas, physiotherapy, bronchodilators
5. Increased renal risk: measure creatinine and blood urea nitrogen levels

COPD, Chronic obstructive pulmonary disease; *ppoDLCO*, predicted postoperative diffusing capacity for carbon monoxide; *ppoFEV*₁, predicted postoperative forced expiratory volume.

BOX 53.6 Final Preanesthetic Assessment for Thoracic Surgery

1. Review initial assessment and test results
2. Assess difficulty of lung isolation: examine chest radiograph and computed tomographic scan
3. Assess risk of hypoxemia during one-lung ventilation

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 before admission to the operating room, they will have to be ordered preoperatively. Consideration for those patients allergic to cephalosporins or penicillin should be made at the time of the initial preoperative visit.

SUMMARY OF THE INITIAL PREOPERATIVE ASSESSMENT

The anesthetic considerations that should be addressed at the time of the initial preoperative assessment are summarized in **Box 53.5**. 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.

FINAL PREOPERATIVE ASSESSMENT

The final preoperative anesthetic assessment for the majority of thoracic surgical patients is carried out immediately before admission of the patient to the operating room. At this time, it is important to review the data from the initial prethoracotomy assessment and the results of tests ordered at that time. In addition, two other specific areas affecting thoracic anesthesia need to be assessed: (1) the potential for difficult lung isolation and (2) the risk of desaturation during OLV (**Box 53.6**).

Difficult Endobronchial Intubation

The most useful predictor of difficult endobronchial intubation is the chest imaging (**Fig. 53.10**).



Fig. 53.10 Preoperative chest radiograph of a 50-year-old woman 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 radiograph but are not mentioned in the radiologist's report. The anesthesiologist must solely examine the chest imaging preoperatively to anticipate problems in lung isolation. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

The anesthesiologist should view the chest imaging before induction of anesthesia because neither the radiologist's nor the surgeon's report of the imaging is made with the specific consideration of lung isolation in mind. Distal airway problems not detectable on the plain chest film can sometimes be visualized on the computed tomography (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 DLT during ventilation of the dependent lung for a left thoracotomy.⁸¹ Similarly, extrinsic compression or intraluminal obstruction of a mainstem bronchus that 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 later in this chapter.

Prediction of Desaturation During One-Lung Ventilation

In the vast majority of cases, it is possible to determine those patients who are most at risk of desaturation during OLV for thoracic surgery. The factors that correlate with desaturation during OLV are listed in **Box 53.7**. In patients at high risk of desaturation, prophylactic measures can be used during OLV to decrease this risk. The most useful prophylactic measures are the use of CPAP (2–5 cm H₂O of oxygen) to the nonventilated lung and/or PEEP to the dependent lung (see "Treatment of Hypoxemia During One-Lung Ventilation").

BOX 53.7 Factors That Correlate With an Increased Risk of Desaturation During One-Lung Ventilation

1. High percentage of ventilation or perfusion to the operative lung on preoperative V/Q scan
2. Poor PaO₂ during two-lung ventilation, particularly in the lateral position intraoperatively
3. Right-sided thoracotomy
4. Normal preoperative spirometry (FEV₁ or FVC) or restrictive lung disease
5. Supine position during one-lung ventilation

FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

The most important predictor of PaO₂ during OLV is the PaO₂ during two-lung ventilation (TLV), specifically the intraoperative PaO₂ during TLV in the lateral position before OLV.⁸² The proportion of perfusion or ventilation to the nonoperated lung on preoperative V/Q scans also correlates with the PaO₂ during OLV.⁸³ If the operative lung has little perfusion preoperatively because of unilateral disease, the patient is unlikely to desaturate during OLV. The side of the thoracotomy has an effect on PaO₂ during OLV. Because the left lung is 10% smaller than the right lung, there is less shunt when the left lung is collapsed. In a series of patients, the mean PaO₂ during left thoracotomy was approximately 70 mm Hg higher than during right thoracotomy.⁸⁴ Finally, the degree of obstructive lung disease correlates in an inverse fashion with PaO₂ during OLV. Other factors being equal, patients with more severe airflow limitation on preoperative spirometry tend to have a better PaO₂ during OLV than patients with normal spirometry (this is discussed later in "Anesthetic Management").⁸⁵

Assessment for Repeat Thoracic Surgery

Patients who survive lung cancer surgery form a high-risk cohort who have a recurrence of the original tumor or develop a second primary tumor. The incidence of developing second primary lung tumors is estimated at 2% per year. The use of routine screening low-dose spiral CT scans probably increases the rate of early detection.⁸⁶ 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.

Intraoperative Monitoring

A few points specific to intraoperative monitoring of the thoracic surgical patient need to be emphasized. The majority of these operations are major procedures of moderate duration (2–4 hours) and are performed with the patient in the lateral position and the hemithorax open. Thus consideration for monitoring and maintenance of body temperature

TABLE 53.4 Intraoperative Complications That Occur With Increased Frequency during Thoracotomy

Complication	Etiology
1. Hypoxemia	Intrapulmonary shunt during one-lung ventilation
2. Sudden severe hypotension	Surgical compression of the heart or great vessels
3. Sudden changes in ventilating pressure or volume	Movement of endobronchial tube/blocker, air leak
4. Arrhythmias	Direct mechanical irritation of the heart
5. Bronchospasm	Direct airway stimulation, increased frequency of reactive airway disease
6. Massive hemorrhage	Surgical blood loss from great vessels or inflamed pleura
7. Hypothermia	Heat loss from the open hemithorax

and fluid volume should be given to all of these cases. Because surgery is usually performed in the lateral position, monitors are initially placed with the patient in the supine position and have to be rechecked and repositioned after the patient is turned. It is difficult to add additional monitoring, particularly invasive vascular monitoring, after the case is started if complications arise. Thus the risk/benefit ratio often tends to favor being overly invasive at the outset. Choice of monitoring should be guided by a knowledge of which complications are likely to occur (Table 53.4).

OXYGENATION

Significant desaturation ($\text{SpO}_2 < 90\%$) during OLV occurs in 1% to 10% of the surgical population in spite of a high FiO_2 (1.0) (see “Management of One-Lung Ventilation” later). Pulse oximetry (SpO_2) has not negated the need for direct measurement of arterial PaO_2 via intermittent blood gases in the majority of thoracotomy patients. The PaO_2 value offers a more useful estimate of the margin of safety above desaturation than the SpO_2 . A patient with a TLV PaO_2 greater than 400 mm Hg with an FiO_2 of 1.0 (or an equivalent $\text{PaO}_2/\text{FiO}_2$ ratio) is unlikely to desaturate during OLV, whereas a patient with a PaO_2 of 200 mm Hg is prone to desaturate during OLV, although both may have SpO_2 values of 99% to 100%.

CAPNOMETRY

The end-tidal CO_2 ($\text{P}_{\text{ET}}\text{CO}_2$) is a less reliable indicator of the PaCO_2 during OLV than during TLV, and the $\text{PaCO}_2-\text{P}_{\text{ET}}\text{CO}_2$ gradient tends to increase during OLV. Although the $\text{P}_{\text{ET}}\text{CO}_2$ is less directly correlated with alveolar minute ventilation during OLV, because the $\text{P}_{\text{ET}}\text{CO}_2$ also reflects lung perfusion and cardiac output, it gives an indication of the relative changes in perfusion of the two lungs independently during position changes and during OLV.⁸⁷ As the patient is turned to the lateral position, the $\text{P}_{\text{ET}}\text{CO}_2$ of the nondependent lung will fall relative to the dependent lung, reflecting increased perfusion of the dependent lung and increased dead space of

the nondependent lung. However, the fractional excretion of CO_2 will be higher from the nondependent lung in most patients because of the increased fractional ventilation of this lung. At the onset of OLV, the $\text{P}_{\text{ET}}\text{CO}_2$ of the dependent lung will usually fall transiently as all of the minute ventilation is transferred to this lung. The $\text{P}_{\text{ET}}\text{CO}_2$ will then rise as the fractional perfusion is increased to this dependent lung by collapse and pulmonary vasoconstriction of the nonventilated lung. If there is no correction of minute ventilation, the net result will be both an increased baseline PaCO_2 and $\text{P}_{\text{ET}}\text{CO}_2$ with an increased gradient. Severe (>5 mm Hg) or prolonged decreases in $\text{P}_{\text{ET}}\text{CO}_2$ can indicate a maldistribution of perfusion between ventilated and nonventilated lungs and may be an early warning of a patient who will subsequently desaturate during OLV.

Invasive Hemodynamic Monitoring

ARTERIAL LINE

There is a significant incidence of transient severe hypotension from surgical compression of the heart or great vessels during intrathoracic procedures. For this reason, plus the utility of intermittent arterial blood gas sampling, it is useful have beat-to-beat assessment of systemic blood pressure during the majority of thoracic surgery cases. Naturally, exceptions occur during limited procedures, such as thoracoscopic resections in younger and healthier patients. For most thoracotomies, placement of a radial artery catheter can be in either the dependent or nondependent arm.

CENTRAL VENOUS PRESSURES

It is a common impression that CVP readings in the lateral position with the chest open are not reliable as a monitor of volume status. The CVP may be a useful monitor postoperatively, particularly for cases where fluid management is critical (e.g., pneumonectomies). A CVP may be required in some cases for vascular access or for vasopressor/inotrope infusions. It is our practice to routinely place CVP lines in pneumonectomy cases, complex procedures, or redo thoracotomies, but not for lesser resections unless there is significant other concurrent illness. Our choice is to use the right internal jugular vein to minimize the risk of pneumothorax for CVP access unless there is a contraindication. Internal jugular CVP data are not reliable in patients with superior vena cava obstruction.

PULMONARY ARTERY CATHETERS

Similar to CVP data, intraoperative pulmonary artery pressure may be a less accurate indicator of true left-heart preload in the lateral position with the chest open than in other clinical situations. This is partly because it is often initially not known if the catheter tip lies in the dependent or nondependent lung. In addition, it is possible that thermodilution cardiac output data may be unreliable if there are significant transient unilateral differences in perfusion between the lungs, as can occur during OLV. There is no consensus on the reliability of thermodilution cardiac output data during OLV.⁸⁸

FIBEROPTIC BRONCHOSCOPY

Placement of DLTs and bronchial blockers is discussed later in the section on Lung Isolation. Significant malpositions of DLTs and blockers that can lead to desaturation during OLV are often not detected by auscultation or other traditional methods of confirming placement.⁸⁹ Placement of DLTs or blockers should be performed with fiberoptic bronchoscopic guidance and should be reconfirmed after placing the patient in the surgical position because a large number of these tubes/blockers migrate during repositioning of the patient.⁹⁰

CONTINUOUS SPIROMETRY

The development of side-stream spirometry has made it possible to continuously monitor inspiratory and expiratory volumes, pressures, and flow interactions during one-lung anesthesia. This monitoring is particularly useful during pulmonary resection surgery. The breath-by-breath monitoring of inspired and expired tidal volumes gives early warning of accidental changes in the intraoperative position of a DLT, with loss of lung isolation if the expired volume suddenly decreases (there is normally a 20- to 30-mL/breath difference caused in part by the uptake of inspired oxygen). The development of a persistent end-expiratory flow during OLV, which correlates with the development of auto-PEEP, can be seen on the flow-volume loop.⁹¹ Also, the ability to accurately measure differences in inspiratory and expiratory tidal volumes is extremely useful in assessing and managing air leaks during and after pulmonary resections.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY

TEE allows the anesthesiologist to have a continuous real-time monitor of myocardial function and cardiac preload. This information is difficult to estimate intraoperatively in the lateral position from other hemodynamic monitors.⁹² Potential indications for intraoperative TEE that apply to thoracic surgery include hemodynamic instability (Fig. 53.11), pericardial effusions, cardiac involvement by tumor, air emboli, pulmonary thromboendarterectomy, thoracic trauma, lung transplantation, and pleuropulmonary disease. A rare cause of hypoxemia associated with thoracic surgery is reversal of shunt flow through an undiagnosed patent foramen ovale. When PEEP (to 15 cm H₂O) was applied during controlled ventilation for nonthoracic surgery, 9% of the patients developed a right-to-left intracardiac shunt.⁹³ TEE should be capable of detecting situations in patients who might intraoperatively develop a right-to-left interatrial shunt during or after thoracic surgery.

Other Monitoring Technology

Cerebral oximetry (SctO₂) has been reported for intraoperative monitoring during OLV.⁹⁴ Elderly, debilitated patients are more likely to experience decreases in SctO₂ during OLV, and these are associated with decreases in SpO₂ and postoperative cognitive dysfunction. However, it has not been shown if any treatment for decreases in SctO₂ affects outcomes.



Fig. 53.11 Midesophageal transesophageal echocardiography (TEE) view of a patient with metastatic breast cancer who had a hemodynamic collapse after induction of general anesthesia for video-assisted thoracoscopic drainage of a left pleural effusion. *TEE* was performed for diagnosis of hemodynamic instability and revealed a previously undiagnosed large pericardial effusion. The “Pericardial Effusion” label shows complete collapse of the right atrium during systole as a result of the effusion, consistent with tamponade. The procedure was modified to include creation of a pericardial window. *LA*, Left atrium; *RV*, right ventricle.

Indirect Cardiac Output

It is not certain that goal-directed fluid therapy using indirect monitors of cardiac output or venous oxygen saturation improves outcomes in abdominal surgery.⁹⁵ At present, the validity of this technology as a valid guide for fluid management when the chest is open remains unclear.

Lung Isolation

Lung-isolation techniques are primarily designed to facilitate OLV in patients undergoing cardiac, thoracic, mediastinal, vascular, esophageal, or orthopedic procedures involving the chest cavity.⁹⁶ Lung isolation is also used to protect the lung from soiling by the contralateral lung in such cases as bronchopleural fistula, pulmonary hemorrhage, and whole-lung lavage. In addition, lung isolation can be used to provide differential patterns of ventilation in cases of unilateral reperfusion injury (after lung transplantation or pulmonary thromboendarterectomy) or in unilateral lung trauma.

Lung isolation can be achieved by three different methods: DLTs, bronchial blockers, or single-lumen endobronchial tubes (SLTs) (Table 53.5). The most common technique is with a DLT. 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 the left lung. The second method involves blockade of a main-stem bronchus to allow lung collapse distal to the occlusion. These bronchial blockers can be used with a standard endotracheal tube (ETT) or contained within a separate channel inside a modified SLT such as the Univent tube (LMA North America, San Diego, CA). The final option for lung isolation is to use either an SLT or endobronchial tube that is advanced into the contralateral mainstem bronchus, protecting this lung while allowing collapse of the lung on the

TABLE 53.5 Options for Lung Isolation

Options	Advantages	Disadvantages
Double-lumen tube 1. Direct laryngoscopy 2. Via tube exchanger 3. Fiberoptically	Easy to place successfully Repositioning rarely required Bronchoscopy to isolated lung Suction to isolated lung CPAP easily added Can alternate OLV to either lung easily Placement still possible if bronchoscopy not available Best device for absolute lung isolation	Size selection more difficult Difficult to place in patients with difficult airways or abnormal tracheas Not optimal for postoperative ventilation Potential laryngeal trauma Potential bronchial trauma
Bronchial blockers (BBs) Arndt Cohen Fuji EZ-Blocker	Size selection rarely an issue Easily added to regular ETT Allows ventilation during placement Easier placement in patients with difficult airways and in children Postoperative two-lung ventilation by withdrawing blocker Selective lobar lung isolation possible CPAP to isolated lung possible	More time needed for positioning Repositioning needed more often Bronchoscope essential for positioning Limited right lung isolation due to RUL anatomy Bronchoscopy to isolated lung impossible Minimal suction to isolated lung Difficult to alternate OLV to either lung
Univent tube	Same as BBs Less repositioning compared with BBs Rarely used	Same as for BBs ETT portion has higher air flow resistance than regular ETT ETT portion has larger diameter than regular ETT
Endobronchial tube	Like regular ETTs, easier placement in patients with difficult airways Longer than regular ETT Short cuff designed for lung isolation	Bronchoscopy necessary for placement Does not allow for bronchoscopy, suctioning, or CPAP to isolated lung Difficult right lung OLV
Endotracheal tube advanced into bronchus	Easier placement in patients with difficult airways	Does not allow for bronchoscopy, suctioning, or CPAP to isolated lung Cuff not designed for lung isolation Extremely difficult right OLV

CPAP, Continuous positive airway pressure; ETT, endotracheal tube; OLV, one-lung ventilation; RUL, right upper lobe.



Fig. 53.12 Photographs of a standard single-lumen endotracheal tube (SLT) (upper left) and a specifically designed SLT (lower left and right). The endobronchial tube is longer and has a shorter cuff. It can be used as an endotracheal tube and advanced into a mainstem bronchus with fiberoptic guidance when needed for lung isolation. (Courtesy Phycon, Fuji Systems Corp., Tokyo, Japan.)

side of surgery (Fig. 53.12). This technique is rarely used today in adult practice (except in some cases of difficult airways, carinal resection, or after a pneumonectomy), owing to the limited access to the nonventilated lung and the difficulty in positioning a standard SLT in the bronchus. This technique is still used when needed in infants and small children: an uncuffed uncut pediatric-size ETT is advanced

into the mainstem bronchus under direct guidance with an infant bronchoscope.

DOUBLE-LUMEN ENDOTRACHEAL TUBES

The design of the Carlens DLT for lung surgery in 1950 was a landmark in the development of thoracic anesthesia

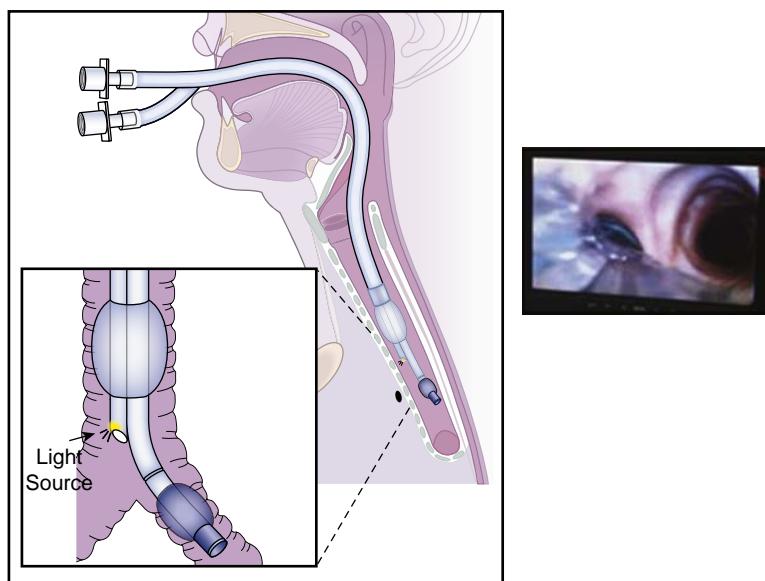


Fig. 53.13 The diagram on the left shows the placement of the VivaSight DLT in the tracheal and left main bronchus. The photograph on the right shows the view of the carina from the camera located beside the light source at the tracheal lumen orifice. *DLT*, Double-lumen tube. (Courtesy ETView Medical.)

because it allowed anesthesiologists to obtain reliable lung isolation in a majority of patients using only laryngoscopy and auscultation. However, the Carlens tube had a high flow resistance owing to the narrow lumina and the carinal hook was difficult to pass through the glottis in some patients. In the 1960s, Robertshaw introduced design modifications for separate left- and right-sided DLTs, removing the carinal hook and using larger lumina. In the 1980s, manufacturers introduced disposable DLTs made of polyvinyl chloride based on the design of the Robertshaw DLT. Among other subsequent improvements is the inclusion of radiographic markers near the endotracheal and endobronchial cuffs and a radiographic marker surrounding the ventilation slot for the right upper lobe bronchus for the right-sided DLT version. Bright blue, low-volume, low-pressure endobronchial cuffs are incorporated for easier visualization during fiberoptic bronchoscopy.

The VivaSight DLT (ETView Medical, Misgav, Israel) has an integrated camera, allowing continuous visualization of its position within the trachea.⁹⁷ This camera is embedded at the end of the endotracheal lumen, so that when connected to a screen monitor via a cable it allows a continuous view of the tracheal carina. In addition, this DLT device has an integrated flushing system that allows for *in situ* camera lens cleaning.⁹⁸ One of the advantages of the VivaSight DLT is that it allows continuous airway monitoring and its view facilitates immediate correction of DLT malpositions at the level of the tracheal carina. In order to maintain a good visualization with the VivaSight camera, it is recommended that a defogging solution be used prior to insertion. **Fig. 53.13** shows the VivaSight DLT and monitor. Some centers have reported that the VivaSight DLT enables more rapid placement when compared to the conventional DLT and may eliminate the need for flexible fiberoptic bronchoscopy in some patients.⁹⁹ However, connecting the camera for prolonged periods of time *in vitro* may lead to melting the portion of the tube near the light source.

The ECOM-DLT (ECOM Medical, Inc., San Juan Capistrano, CA) contains multiple electrodes on the cuff and the tube that continuously measure the bioimpedance signal from the ascending aorta, in close proximity to the trachea. This device when connected to the ECOM monitor, in conjunction with an arterial catheter, provides cardiac output measurements (**Fig. 53.14**). This new ECOM-DLT has not been compared to other technology; however based on the original ECOM ETT,¹⁰⁰ it appears to be promising to derive hemodynamic parameters while in thoracic surgical patients.

Fuji Systems (Tokyo, Japan) has introduced the Silbroncho DLT, which is made of silicone. The unique characteristic of this device relies on the flexible wire-reinforced endobronchial tip. In addition, there is a beveled bronchial orifice and reduced bronchial cuff length that should increase the margin of safety when compared with other designs of DLTs. The Silbroncho DLT is particularly useful for performing a tube exchange from a single- to a double-lumen tube in combination with a video-laryngoscope and a tube exchange catheter (see “Difficult Airways and One-Lung Ventilation” later).¹⁰¹

Size Selection

Table 53.6 lists the different sizes of DLT, the appropriate fiberoptic bronchoscope sizes to be used, and the comparable diameters of SLTs. A properly sized, left-sided DLT should have a bronchial tip 1 to 2 mm smaller than the patient’s left bronchus diameter to allow for the space occupied by the deflated bronchial cuff. A study by Eberle and associates¹⁰² used a three-dimensional image reconstruction of tracheobronchial anatomy from the spiral CT scans combined with superimposed transparencies of DLTs to predict proper size for a right- or left-sided DLT. Chest radiographs and CT scans are valuable tools for selection of proper DLT size in addition to their proven value in assessment of abnormal tracheobronchial anatomy and should be reviewed before the placement of the DLT (**Fig. 53.15**). A multidetector CT

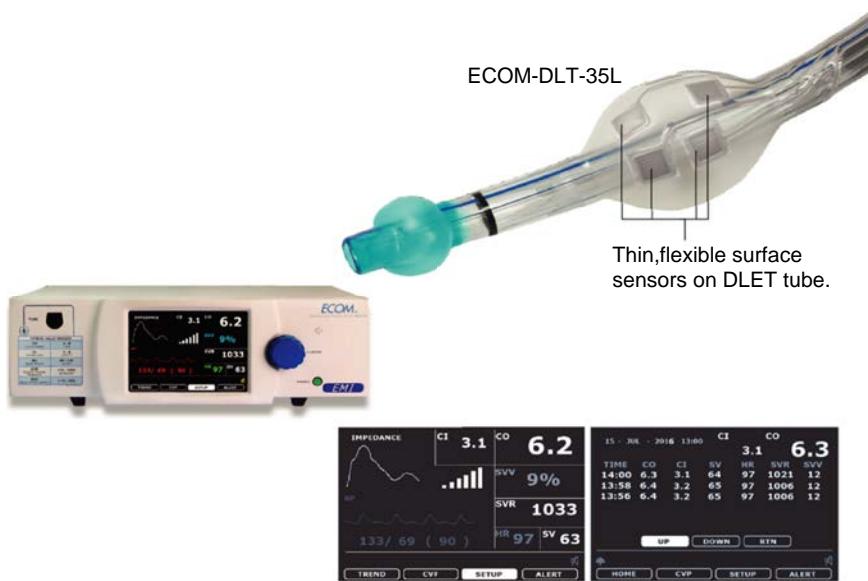


Fig. 53.14 The ECOM DLT has multiple electrodes on the cuff and the tube that continuously measure the bioimpedance signal from the ascending aorta with measurements of cardiac output. *DLT*, Double-lumen tube. (Courtesy ECOM Medical, Inc., San Juan Capistrano, CA)

TABLE 53.6 Comparative Diameters of Single- and Double-Lumen Tubes

SINGLE-LUMEN TUBES		DOUBLE-LUMEN TUBES			
Internal Diameter (ID) (mm)	External Diameter (ED) (mm)	French Size (Fr)	Double-lumen ED (mm)	Bronchial Lumen ID (mm)	FOB size (mm)
6.5	8.9	26	8.7	3.2	2.4
7.0	9.5	28	9.3	3.4	2.4
8.0	10.8	32	10.7	3.5	2.4
8.5	11.4	35	11.7	4.3	≥3.5
9.0	12.1	37	12.3	4.5	≥3.5
9.5	12.8	39	13.0	4.9	≥3.5
10.0	13.5	41	13.7	5.4	≥3.5

ED, External diameter; *FOB*, fiberoptic bronchoscope; *ID*, internal diameter.

Double-lumen ED = the approximate external diameter of the double-lumen portion of the tube. *FOB* size = the maximal diameter of fiberoptic bronchoscope that will pass through both lumens of a given size of double-lumen tube.

scan (MDCT) of the chest allows appreciation of any abnormal tracheobronchial anatomy before placement of a DLT. A simplified method of selection of DLT size is given in Table 53.7. It is important to appreciate that compared with SLTs, DLTs have a large external diameter (Fig. 53.16) and they should not be advanced against significant resistance.

Methods of Insertion

Two techniques are commonly used when inserting and placing a DLT. One is the blind technique: the DLT is passed with direct laryngoscopy and then turned 90 degrees counterclockwise (for a left-sided DLT placement) after the endobronchial cuff has passed beyond the vocal cords. The DLT should pass the glottis without any resistance. Seymour¹⁰³ showed that the mean diameter of the cricoid ring is approximately the same as that of the left mainstem bronchus. The optimal depth of insertion for a left-sided DLT is correlated

with the patient's height in average-sized adults. In adults, depth, measured at the teeth, for a properly positioned DLT, will be approximately $12 + (\text{patient height}/10)$ cm.¹⁰⁴ In patients of Asian descent, many of whom are of shorter stature (<155 cm), patient height is not a good predictor of depth of insertion of a DLT.¹⁰⁵ An inadvertently deep insertion of a DLT can lead to serious complications, including rupture of the left mainstem bronchus. Fig. 53.17 depicts the blind method technique for insertion of a left-sided DLT.

The direct vision technique uses bronchoscopic guidance, in which the tip of the endobronchial lumen is guided into the correct bronchus after the DLT passes the vocal cords using direct vision with a flexible fiberoptic bronchoscope. A study by Boucek and associates¹⁰⁶ comparing the blind technique versus fiberoptic bronchoscopy-guided technique showed that of the 32 patients who underwent the blind technique approach, primary success occurred in 27 patients and eventual success occurred in 30 patients. In contrast, in the 27 patients using the bronchoscopy-guided technique, primary success was achieved only in 21 patients and eventual success in 25 patients. Although both methods resulted in successful left mainstem bronchus placement in all patients, more time was required when fiberoptic bronchoscopy guidance technique was used (181 vs. 88 seconds).

Videolaryngoscopy is an important technique in the management of patients with expected or unexpected difficult airways. Clinical studies have shown that videolaryngoscopes improve visualization of laryngeal structures and facilitate insertion of a single-lumen ETT.¹⁰⁷ The use of the C-MAC videolaryngoscope has been compared with the Macintosh blade (the most common device used during laryngoscopy with a DLT) and the Miller blade during DLT intubation in patients with normal airways. The authors of this retrospective study showed that videolaryngoscopy views were similar to the views obtained with a Miller blade while passing a DLT.¹⁰⁸ In contrast the group that used a Macintosh blade had reported higher difficult intubations with the DLTs. A study comparing the GlideScope

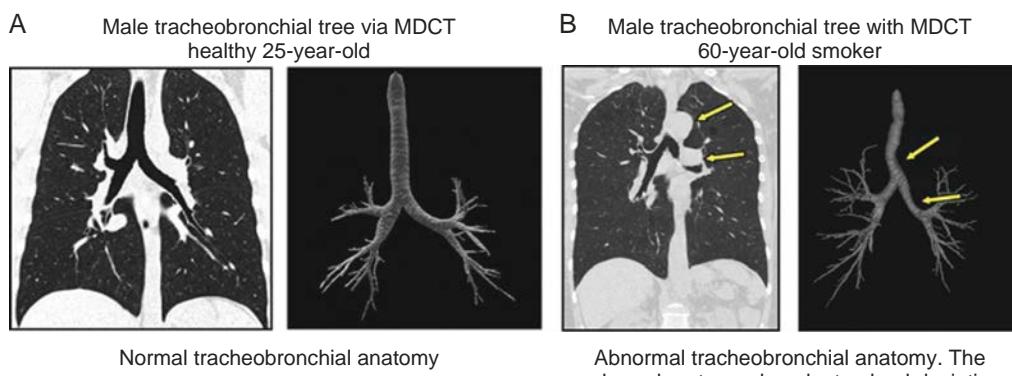


Fig. 53.15 (A) The multidetector CT scan and also three-dimensional view of tracheobronchial anatomy in a healthy volunteer. (B) Abnormal tracheobronchial anatomy in a 60-year-old smoker. The arrows show enlarged aorta (left) and the deviation of the trachea toward the right caused by the enlarged aorta (right). *CT*, Computed tomography.

TABLE 53.7 Selection of Double-Lumen Tube Size Based on Adult Patient's Sex and Height

Sex	Height (cm)	Size of Double-Lumen Tube (Fr)
Female	<160 (63 in)*	35
Female	>160	37
Male	<170 (67 in)**	39
Male	>170	41

*For females of short stature (<152 cm or 60 in), examine bronchial diameter on computed tomographic scan, consider 32-Fr double-lumen tube.

**For males of short stature (<160 cm), consider 37-Fr double-lumen tube.

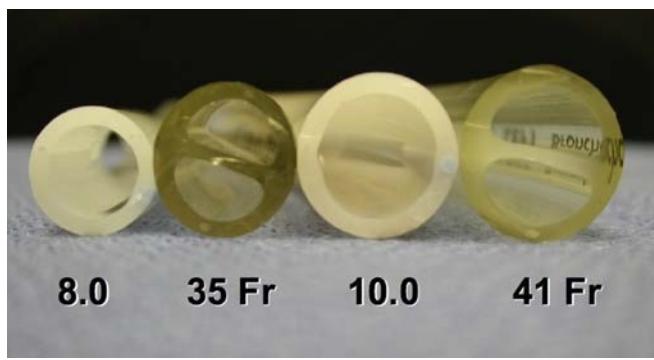


Fig. 53.16 Photograph of the cut cross sections of several SLTs and DLTs. The external diameter of a 35-Fr DLT is larger than that of an 8.0-mm (internal diameter) SLT, and a 41-Fr DLT is larger than a 10-mm SLT. *DLT*, Double-lumen tube; *SLT*, single-lumen tube. (Photo courtesy Dr. J Klafta.)

videolaryngoscope and the Macintosh direct laryngoscope for DLT intubation in patients with normal airways showed that the overall ease of successful intubation was higher with the Macintosh blade compared with the GlideScope¹⁰⁹; also voice changes were less common in the Macintosh group. Therefore the authors do not recommend the routine use of the GlideScope in patients who have normal airways while using a DLT. In contrast, a study using the Airtraq DL videolaryngoscope during placement of DLT showed an improvement in exposure of the supraglottis during insertion of the DLT in patients with normal airways.¹¹⁰ The usefulness of a videolaryngoscope while inserting a DLT will

depend on the experience of the operator and the individual anatomy of the patient's airway.

RIGHT-SIDED DOUBLE-LUMEN ENDOBRONCHIAL TUBES

Although a left-sided DLT is used more commonly for most elective thoracic procedures,¹¹¹ there are specific clinical situations in which the use of a right-sided DLT is indicated (Box 53.8). The anatomic differences between the right and the left mainstem bronchus are reflected in the 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 to 2 cm from the carina, techniques using right endobronchial intubation must take into account the location and potential for obstruction of the orifice of the right upper lobe bronchus. The right-sided DLT incorporates a modified cuff and slot on the endobronchial lumen that allows ventilation for the right upper lobe (Fig. 53.18).¹¹²

Positioning of Double-Lumen Tubes

Auscultation alone is unreliable for confirmation of proper DLT placement. Auscultation (Fig. 53.19) and bronchoscopy should both be used each time a DLT is placed and again when the patient is repositioned. Fiberoptic bronchoscopy is performed first through the tracheal lumen to ensure that the endobronchial portion of the DLT is in the left bronchus and that there is no bronchial cuff herniation over the carina after inflation. Through the tracheal view, the blue endobronchial cuff ideally should be seen approximately 5 to 10 mm below the tracheal carina in the left bronchus. It is crucial to identify the take-off of the right upper lobe bronchus through the tracheal view. Going inside this right upper lobe with the bronchoscope should reveal three orifices (apical, anterior, and posterior). This is the only structure in the tracheobronchial tree that has three orifices. In the supine patient, the take-off of the right upper lobe is normally on the lateral wall of the right mainstem bronchus at the 3- to 4-o'clock position in relation to the main carina. Broncho-Cath tubes from Mallinckrodt have a radiopaque line encircling the tube. This line is proximal to the bronchial cuff and can be useful

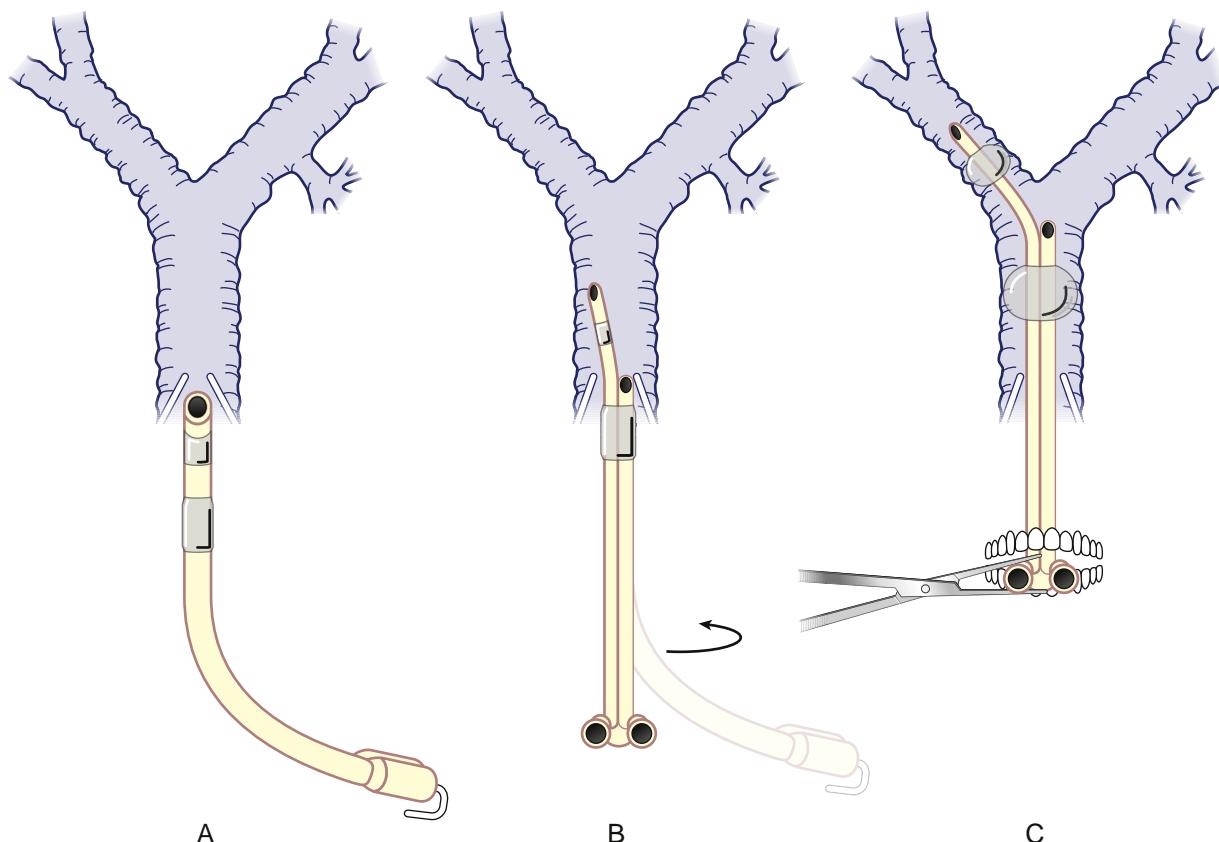


Fig. 53.17 Blind method for placement of a left-sided DLT. (A) The DLT is passed with direct laryngoscopy beyond the vocal cords. (B) The DLT is rotated 90 degrees to the left (counter-clockwise). (C) The DLT is advanced to an appropriate depth (in general 27-29 cm marking at the level of the teeth). *DLT*, Double-lumen tube. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

BOX 53.8 Indications for a Right-Sided Double-Lumen Tube

- Distorted anatomy of the entrance of left mainstem bronchus
 - External or intraluminal tumor compression
 - Descending thoracic aortic aneurysm
- Site of surgery involving the left mainstem bronchus
 - Left lung transplantation
 - Left-sided tracheobronchial disruption
 - Left-sided pneumonectomy*
 - Left-sided sleeve resection

*It is possible to manage a left pneumonectomy with a left-sided DLT or bronchial blocker; however, the DLT or blocker will have to be withdrawn before stapling the left mainstem bronchus.

This is a common clinical practice pattern for using right-sided double-lumen tubes (DLTs) and assumes normal tracheobronchial anatomy, specifically a normal position of the orifice of the right upper lobe; however, some clinicians prefer to use right DLTs for all left-sided surgeries.

while positioning a left-sided DLT. The radiopaque marker is 4 cm from the distal tip of the endobronchial lumen. This marker reflects white during fiberoptic visualization and, when positioned slightly above the tracheal carina, should provide the necessary margin of safety for positioning into the left mainstem bronchus.¹¹³ The next observation with the fiberoptic bronchoscope is made through the endobronchial lumen to check for patency of the tube and

determination of margin of safety. The orifices of both the left upper and lower lobes must be identified to avoid distal impaction in the left lower lobe and occlusion of the left upper lobe (Fig. 53.20). Fig. 53.21 displays the tracheobronchial anatomy along with fiberoptic bronchoscopy findings from the endotracheal or endobronchial lumen for a left-sided DLT.

Problems Related to Double-Lumen Tubes

The most common problems and complications associated with the use of a DLT are malposition and airway trauma. A malpositioned DLT will fail to allow collapse of the lung, causing gas trapping during positive-pressure ventilation, or it may partially collapse the ventilated or dependent lung, producing hypoxemia. A common cause of malposition is dislodgment of the endobronchial cuff because of overinflation, surgical manipulation of the bronchus, or extension of the head and neck during or after patient positioning. Fiberoptic bronchoscopy is the recommended method to diagnose and correct intraoperative malposition of DLTs along with proper recognition of tracheobronchial anatomy. If a DLT is malpositioned in the supine or lateral decubitus position, there is a greater likelihood of hypoxemia during OLV. If a DLT is in the optimal position, but lung deflation is not completely achieved, a suction catheter should be passed to the side where lung collapse is supposed to occur. This suction will expedite lung deflation. The suction catheter must then be removed to avoid including it in a suture line.

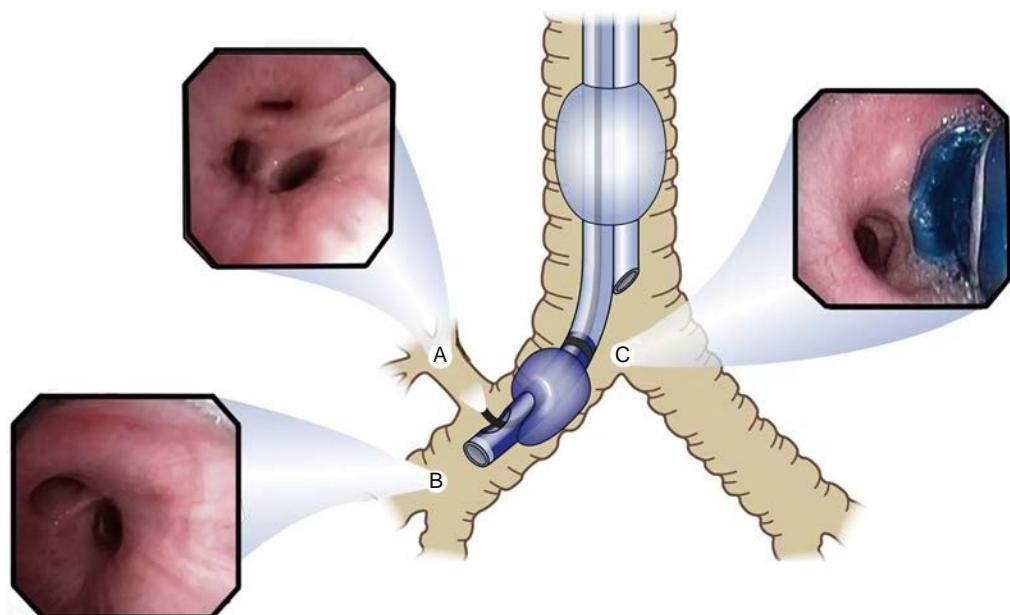


Fig. 53.18 Fiberoptic bronchoscopic examination of a Rusch right-sided DLT. (A) Slot of the bronchial lumen properly aligned within the entrance of the right upper lobe bronchus. (B) Part of the bronchus intermedius when the bronchoscope is advanced through the distal portion of the bronchial lumen. (C) Edge of the bronchial cuff at the entrance of the right mainstem bronchus when the bronchoscope is passed through the tracheal lumen. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

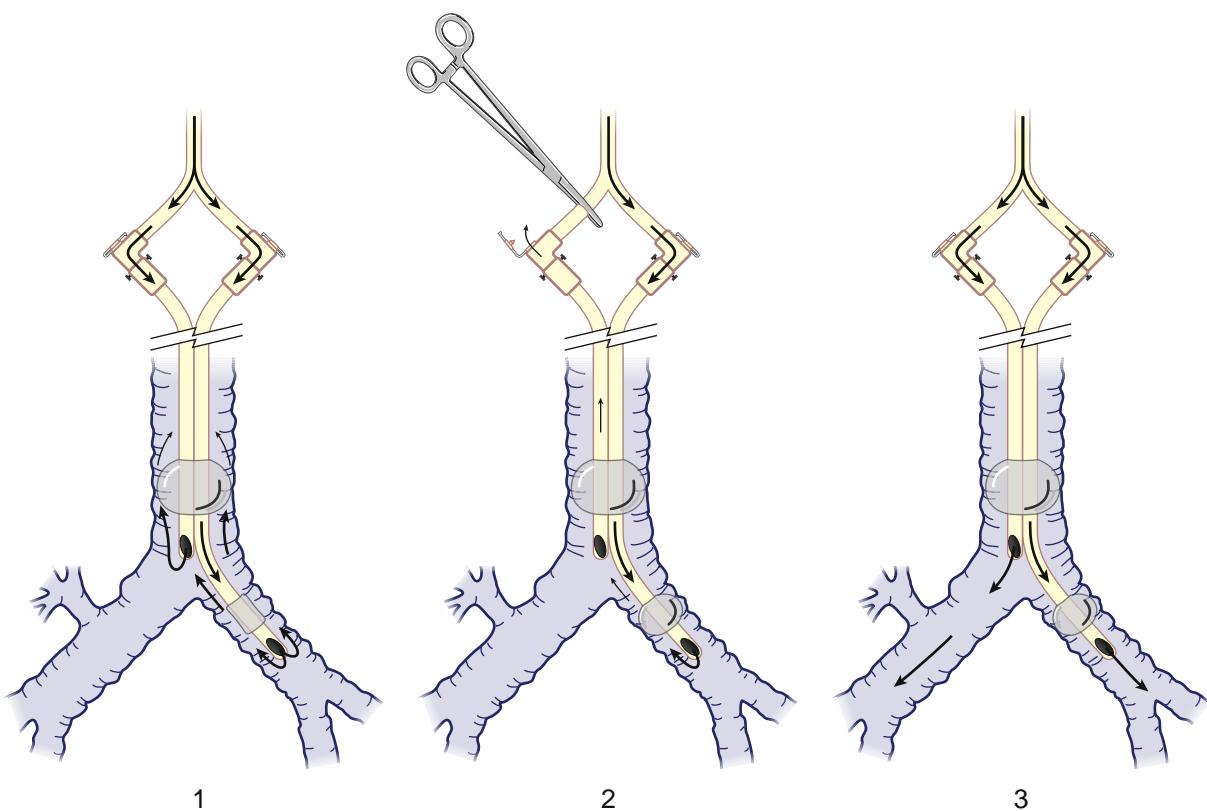


Fig. 53.19 A “3-step” method to confirm position of a left DLT by auscultation. Step 1, During bilateral ventilation, the tracheal cuff is inflated to the minimal volume that seals the air leak at the glottis. Auscultate to confirm bilateral ventilation. Step 2, The tracheal lumen of the DLT is clamped proximally (“clamp the short side short”) and the port distal to the clamp is opened. During ventilation via the bronchial lumen, the bronchial cuff is inflated to the minimal volume that seals the air leak from the open tracheal lumen port. Auscultate to confirm correct unilateral ventilation. Step 3, The tracheal lumen clamp is released and the port is closed. Auscultate to confirm resumption of bilateral breath sounds. DLT, Double-lumen tube. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

Airway trauma and rupture of the membranous part of the trachea or the bronchus is a potential complication with the use of DLTs.¹¹⁴ Airway trauma can occur from an oversized DLT or when an undersized DLT migrates distally into the lobar bronchus and the main (i.e., tracheal) body of the DLT comes into the bronchus, producing lacerations

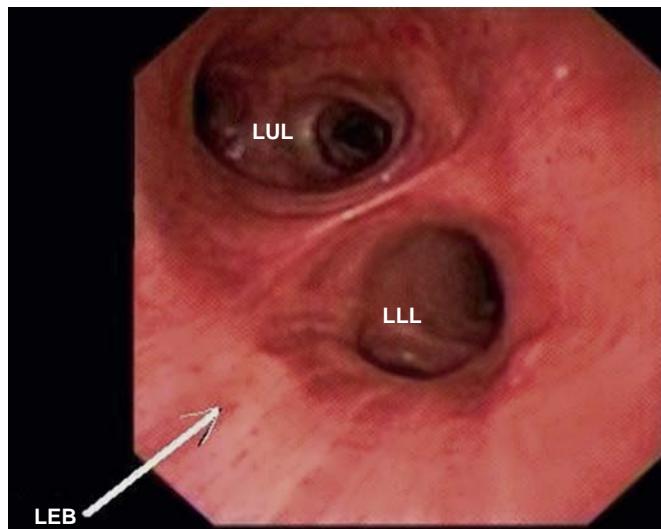


Fig. 53.20 The view from the distal bronchial lumen of a well-positioned left-sided DLT. Both the orifices of the left upper lobe (LUL) and left lower lobe (LLL) can be identified. Note the longitudinal elastic bundles (LEB, arrow). These extend down the posterior membranous walls of the trachea and mainstem bronchi. They are useful landmarks to orient the bronchoscopist to anterior-posterior directions. In the left mainstem bronchus, they extend into the left lower lobe and are a useful landmark to distinguish the lower from the upper lobe. DLT, Double-lumen tube.

or rupture of the airway. Airway damage during the use of DLTs can present as an unexpected air leak, subcutaneous emphysema, massive airway bleeding into the lumen of the DLT, or protrusion of the endotracheal or endobronchial cuffs into the surgical field, with visualization of this by the surgeon. If any of the aforementioned problems occur, a bronchoscopic examination and surgical repair should be performed. Another potential problem is the development of a tension pneumothorax in the dependent, ventilated lung during OLV.¹¹⁵

BRONCHIAL BLOCKERS

An alternative method to achieve lung separation involves blockade of a mainstem bronchus to allow lung collapse distal to the occlusion (Fig. 53.22). Bronchial blockers also can be used selectively to achieve lobar collapse if necessary. Currently, there are several different bronchial blockers available to facilitate lung separation. These devices are either within a modified SLT as an enclosed bronchial blocker (Torque Control Blocker Univent; Vitaid, Livingston, NY) or are used independently with a conventional SLT, such as the Arndt wire-guided endobronchial blocker (Cook Critical Care, Bloomington, IN), the Cohen tip-deflecting endobronchial blocker (Cook Critical Care), the Fuji Uniblocker (Vitaid), and the EZ-Blocker (Teleflex, Dresden, Germany).

There are specific conditions in which a bronchial blocker may be preferred to a DLT, such as patients with previous oral or neck surgery who present with a challenging airway and require lung separation for intrathoracic surgery. In these cases, the use of an SLT during an awake nasotracheal or orotracheal intubation or via tracheostomy secures the

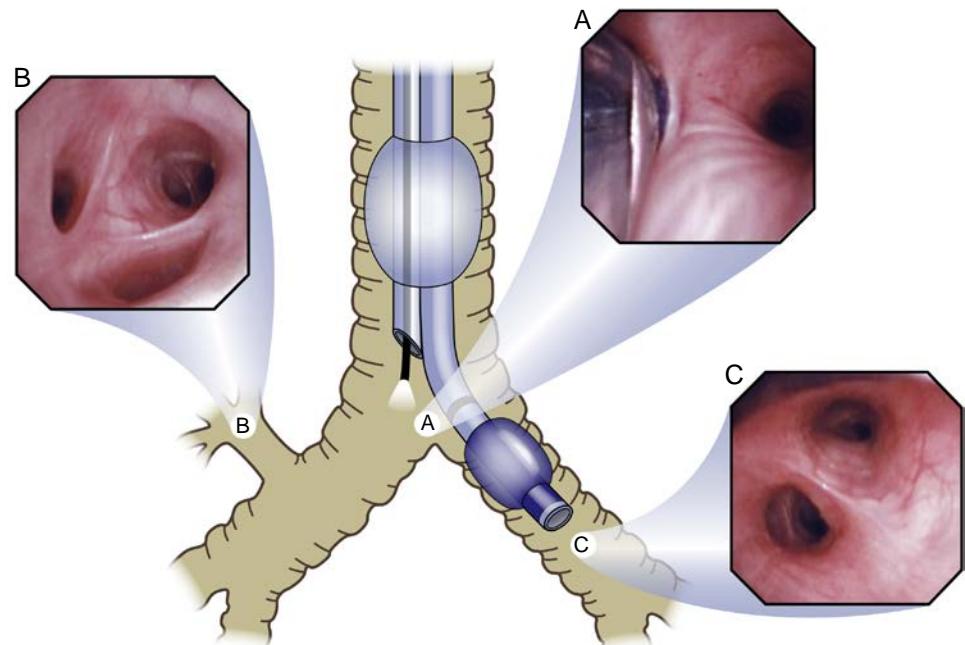


Fig. 53.21 Fiberoptic bronchoscopic examination of a Mallinckrodt left-sided DLT. (A) The edge of the endobronchial cuff around the entrance of the left mainstem bronchus when the bronchoscope is passed through the tracheal lumen. A white line marker is seen above the tracheal carina. (B) Clear view of the right upper lobe bronchus and its three orifices: apical, anterior, and posterior segments. (C) A clear view of the bronchial bifurcation (left upper and left lower bronchi) when the left-sided DLT is in the optimal position and the fiberoptic bronchoscope is being advanced through the endobronchial lumen. DLT, double-lumen tube. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

airway, and thereafter an independent bronchial blocker can be placed to achieve lung separation. Another group of patients who may benefit from the use of bronchial blockers are those cancer patients who have undergone a previous contralateral pulmonary resection. In such cases, selective lobar blockade with a bronchial blocker in the ipsilateral side improves oxygenation and facilitates surgical exposure. Blockers can be advanced over a guidewire placed with a fiberoptic bronchoscope into the required lobar bronchus. Bronchial blockers are most commonly used intraluminally (coaxially) with the SLT. The Cohen and Fuji Uniblockers can also be placed separately through the glottis or tracheostomy exterior to the SLT. This allows the use of a smaller SLT and is often an option in pediatrics. Another advantage of the bronchial blockers is when postoperative mechanical ventilation is being considered after prolonged thoracic or esophageal surgery. In many instances, these patients have an edematous upper airway at the end of the procedure. If a bronchial blocker is used, there is no need to change the SLT and there is no compromise of the airway if mechanical ventilation is needed in the postoperative period. **Table 53.8** describes the characteristics of current bronchial blockers. The smallest internal diameter (ID) of an ETT that will allow passage of both a bronchial blocker and a fiberoptic

bronchoscope depends on the diameters of the bronchoscope and blocker. For standard adult 9-Fr blockers, an ETT greater than or equal to 7.0 mm ID can be used with a bronchoscope less than 4.0 mm in diameter. Larger bronchoscopes will require an ETT greater than 7.5 mm ID. All blockers need to be well lubricated before placement.

Wire-Guided Endobronchial Blocker (Arndt Blocker)

Fig. 53.23A displays the Arndt blockers. The Arndt blocker has a retractable loop that is placed over the fiberoptic bronchoscope, which is then used to guide the blocker into place. The Arndt blockers usually advance easily into the right mainstem bronchus without the loop.

Cohen Endobronchial Blocker

The Cohen blocker (see **Fig. 53.23B**, left blocker) uses a wheel located in the most proximal part of the unit that deflects the tip of the distal part of the blocker into the desired bronchus. This blocker has been preangled at the distal tip to facilitate insertion into a target bronchus. On the distal shaft above the balloon, there is an arrow that, when seen with the fiberoptic bronchoscope, indicates in which direction the tip deflects. To position the Cohen blocker, the arrow is aligned with the

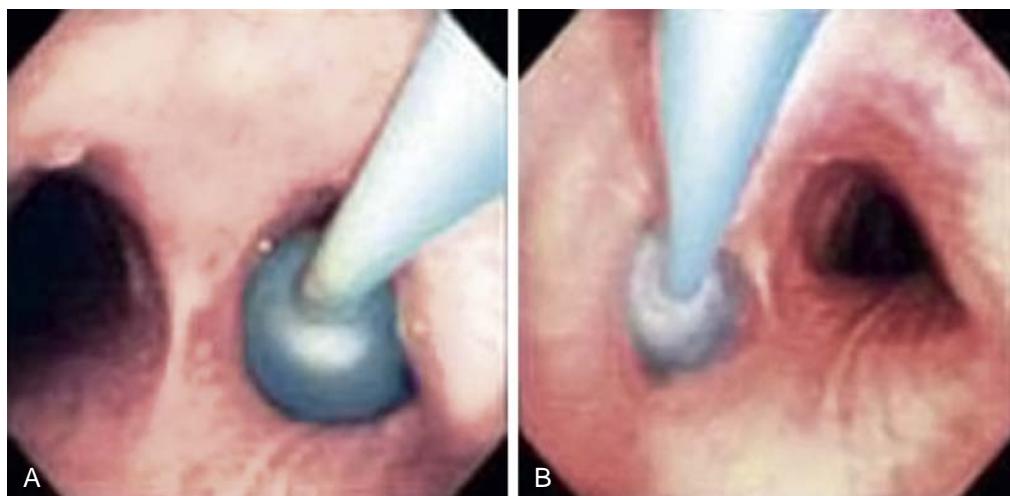


Fig. 53.22 Placement of a bronchial blocker. In the photos, correct positioning of a blocker in the right (A) and left (B) mainstem bronchi as seen through a fiberoptic bronchoscope just above the carina in the trachea. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

TABLE 53.8 Characteristics of the Cohen, Arndt, Fuji, and EZ Bronchial Blockers

	Cohen Blocker	Arndt Blocker	Fuji Uniblocker	EZ-Blocker
Size	9-Fr	5-Fr, 7-Fr, and 9-Fr	5-Fr, 9-Fr	7-Fr
Balloon shape	Spherical	Spherical or elliptical	Spherical	Spherical \times 2
Guidance mechanism	Wheel device to deflect the tip	Nylon wire loop that is coupled with the fiberoptic bronchoscope	None, preshaped tip	None
Smallest recommended ETT for coaxial use	9-Fr (8.0 ETT)	5-Fr (4.5 ETT), 7-Fr (7.0 ETT), 9-Fr (8.0 ETT)	9-Fr (8.0 ETT)	7.5 ID
Murphy eye	Present	Present in 9-Fr	Not present	No
Center channel	1.6 mm ID	1.4 mm ID	2.0 mm ID	1.4 mm ID

ETT, Endotracheal tube; ID, internal diameter.

Modified from Campos JH: Which device should be considered the best for lung isolation: Double-lumen endotracheal tube versus bronchial blockers. *Curr Opin Anaesthesiol*. 2007;20:30, with permission.

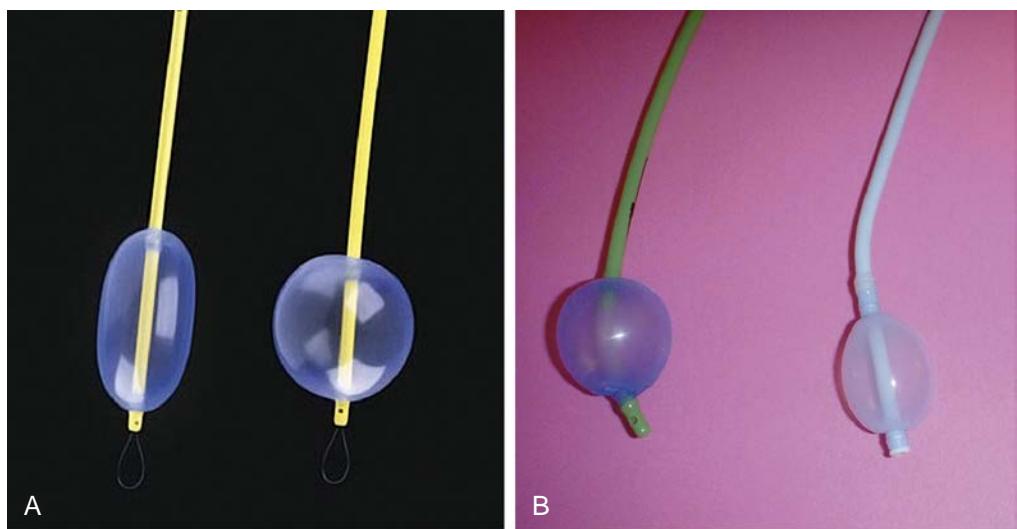


Fig. 53.23 (A) The original elliptical (left) and the newer spherical Arndt designs of bronchial blocker (Cook Critical Care, Bloomington, IN). (B) The Cohen (left) (Cook Critical Care, Bloomington, IN) and Fuji Uniblocker (right) (Vitaids, Lewiston, NY) bronchial blockers.

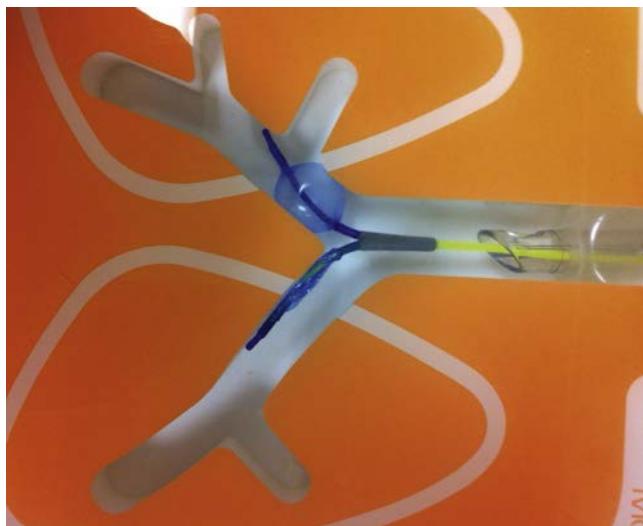


Fig. 53.24 The EZ-Blocker (Rusch, Teleflex) has two distal limbs each with a blocker-balloon that are positioned in each mainstem bronchus and is fixed at the carina. The two limbs are color-coded (blue and yellow) and the appropriate blocker is inflated via a matching colored pilot balloon.

bronchus to be intubated, the proximal wheel is turned to deflect the tip toward the desired side, and then the blocker is advanced with fiberoptic guidance.

Fuji Uniblocker

The Fuji Uniblocker (see Fig. 53.22B, right blocker) is an independent blocker that is made of silicone material and has a simple, fixed distal hockey-stick angulation to facilitate insertion. The blocker is simply rotated to the left or right as needed under fiberoptic bronchoscope guidance for placement in the required bronchus.

EZ-Blocker

The EZ-blocker (Fig. 53.24) is a recently introduced 7-Fr, 4-lumen catheter with a Y-shaped bifurcation. Each distal end has a balloon that can be guided into the right and left main bronchus. This device comes with its own multiport

adaptor and is used through a 7.5 SLT. The end of the Y sits on the tracheal carina. Each distal end is positioned into the right and left bronchus, and the bronchial balloon is inflated in the operative side for lung isolation.

Complications Related to the Bronchial Blockers

Failure to achieve lung separation because of abnormal anatomy or lack of a seal within the bronchus has been reported.¹¹⁶ Inclusion of the bronchial blocker or the distal wire loop of an Arndt blocker into the stapling line has been reported during a lobectomy¹¹⁷ and required surgical reexploration after unsuccessful removal of the bronchial blocker after extubation. To avoid these mishaps, communication with the surgical team regarding the presence of a bronchial blocker in the surgical side is crucial. Clearly, the bronchial blocker needs to be withdrawn a few centimeters before stapling.

Another potentially dangerous complication with all bronchial blockers is that the inflated balloon may move and lodge above the carina or be accidentally inflated in the trachea. This leads to an inability to ventilate, hypoxia, and potentially cardiorespiratory arrest unless quickly recognized and the blocker deflated.¹¹⁸ There is a report of more malpositions with the use of bronchial blockers when compared to DLTs.¹¹⁹

In a retrospective review of 302 consecutive cases from a single institution, no major complications were found with the use of different bronchial blockers during lung isolation.¹²⁰ A recent report described three cases where the balloon of the Fuji blocker failed to deflate at the conclusion of the surgery. In two of the cases, the already inflated bronchial blocker had to be removed along with the single-lumen ETT during extubation.¹²¹ It is our recommendation to test the pilot and the balloon prior to use to ensure that the air that is injected is aspirated and the balloon completely deflates.

Difficult Airways and One-Lung Ventilation

A number of patients requiring OLV are identified during preoperative evaluation to have a potentially difficult airway.¹²² Others present with unexpected difficulty to

intubate after induction of anesthesia. Between 5% and 8% of patients with primary lung carcinoma also have a carcinoma of the pharynx, usually in the epiglottic area.¹²³ 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 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. Such anomalies can be detected by reviewing the chest radiographs and CT scans of the chest. A flexible fiberoptic bronchoscopic examination is necessary to assess a distorted area of the airway before selection of a specific tube or blocker to achieve OLV.

In patients who require OLV and present with a difficult airway, the primary goal is to establish an airway with an SLT placed orally with the aid of a flexible fiberoptic bronchoscope, after appropriate airway anesthesia is achieved. In selected patients who seem easy to ventilate, this may be performed after induction of anesthesia with a bronchoscope or with a videolaryngoscope.¹²⁴ Once the SLT is in place, an independent bronchial blocker can be passed. If the patient requires OLV and cannot be intubated orally, an awake nasotracheal intubation can be performed with an SLT and, once the airway is established, then a bronchial blocker can be used.

An alternative to achieve OLV in a patient with a difficult airway is to intubate the patient's trachea with an SLT; then a DLT-SLT tube-exchange catheter can be used to replace the existing SLT with a DLT after general anesthesia is induced. For a DLT the exchange catheter should be at least 83 cm. A 14-Fr exchange catheter can be used for 41-Fr and 39-Fr DLTs; for 37-Fr or 35-Fr DLTs an 11-Fr exchange catheter is used. Specially designed exchange catheters for DLTs are available with a softer distal tip to try to decrease the risk of distal airway trauma (e.g., Cook Exchange Catheter, Cook Critical Care).

The exchange catheter, SLT, and the DLT combination should be tested in vitro before the exchange. A sniffing position facilitates tube exchange. After the exchange catheter is lubricated, it is advanced through an SLT. The catheter should not be inserted deeper than 24 cm at the lips to avoid accidental rupture or laceration of the trachea or bronchi. After cuff deflation, the SLT is withdrawn. Then the endobronchial lumen of the DLT is advanced over the exchange catheter. It is optimal to use a videolaryngoscope during the tube exchange to guide the DLT through the glottis under direct vision (Fig. 53.25). If a videolaryngoscope is not available, having an assistant perform standard laryngoscopy during tube exchange partially straightens out the alignment of the oropharynx and glottis and facilitates the exchange. Proper final position of the DLT is then achieved with auscultation and bronchoscopy.

Lung-Isolation Techniques in Patients With a Tracheostomy in Place

Placement of a DLT through a tracheostomy stoma may be prone to malposition because the upper airway has



Fig. 53.25 A DLT is placed over a tube-exchange catheter using a video laryngoscope for guidance. The green SLT-DLT tube-exchange catheter (Cook Critical Care, Bloomington, IN) was passed initially through the SLT, which has been withdrawn (before the photo was taken) and the catheter then passed retrograde through the bronchial lumen of a DLT, which is advanced under direct vision through the glottis. The DLT in this picture (Fuji, Phycon, Vitaaid, Lewiston, NY) has a bevel on the distal bronchial orifice and a flexible bronchial lumen that facilitates this procedure. *DLT*, Double-lumen tube; *SLT*, single-lumen tube.

been shortened and the conventional DLT may be too long. Before placing any lung isolation devices through a tracheostomy stoma it is important to consider whether it is a fresh stoma (i.e., a few days old, when the airway can be lost immediately on decannulation) versus a chronic tracheostomy. The alternatives to achieve OLV in a tracheostomized patient include (1) insertion of an SLT followed by an independent bronchial blocker passed coaxially or externally to the SLT¹²⁵; (2) the use of a disposable cuffed tracheostomy cannula with an independent bronchial blocker; (3) replacement of the tracheostomy cannula with a specially designed short DLT such as the Naruke DLT, which is made for use in tracheostomized patients¹²⁶; (4) placement of a small DLT through the tracheostomy stoma; or (5) if possible, oral access to the airway for standard placement of a DLT or blocker (this is occasionally an option in patients on prolonged mechanical ventilation for respiratory failure or postoperative complications).

In summary, the optimal method of lung isolation will depend on a number of factors, including the patient's airway anatomy, the indication for lung isolation, the available equipment, and the training of the anesthesiologist. Whatever method of lung isolation is used, the "ABCs" of lung isolation are:

Anatomy. Know the tracheobronchial anatomy. One of the major problems that many anesthesiologists have in achieving satisfactory lung isolation is due to lack of familiarity with distal airway anatomy (Fig. 53.26).

Bronchoscopy. Whenever possible use a fiberoptic bronchoscope to position endobronchial tubes and blockers. The ability to perform fiberoptic bronchoscopy is now a fundamental skill needed by all anesthesiologists providing anesthesia for thoracic surgery. An online bronchoscopy simulator has been developed to help train anesthesiologists in positioning DLTs and blockers. This simulator, which uses real-time video, is available without cost at www.thoracicanesthesia.com.

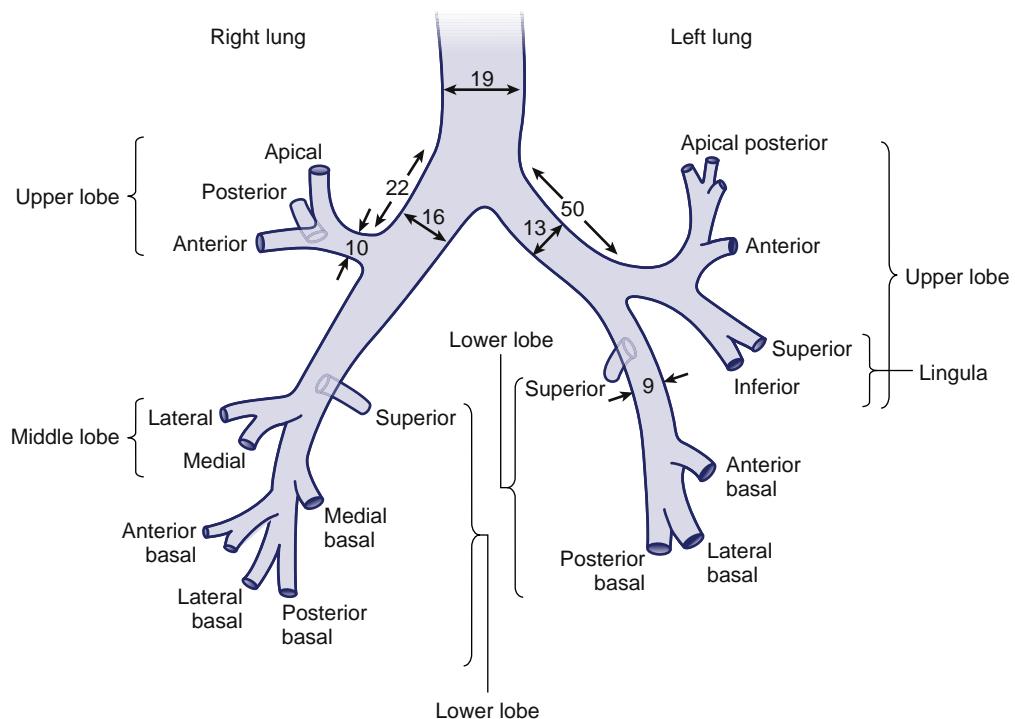


Fig. 53.26 Diagram of the tracheobronchial tree. Mean lengths and diameters are shown in millimeters. Note that the right middle lobe bronchus exits directly anteriorly and the superior segments (some authors refer to these as the “apical” segments) of the lower lobes exit directly posteriorly. Using the apical designation, on the right side the segmental bronchi in a rostral to caudal sequence give the mnemonic “A PALM A MAPL”. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

Chest imaging. The anesthesiologist should always look at the chest imaging before placement of a DLT or blocker. Abnormalities of the lower airway can often be identified in advance, and this will have an impact on the selection of the optimal method of lung isolation for a specific case (see Figs. 53.10 and 53.15).

POSITIONING

The majority of thoracic procedures are performed in the lateral position, most often the lateral decubitus position, but depending on the surgical technique a supine, semisupine or semiprone lateral position may be used. These 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. 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 and the diseased lung turned to the nondependent side.

Because of 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 responsibility for the head, neck, and airway during position change and must be in charge of the 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 after repositioning. It is nearly impossible to avoid some movement of a DLT or bronchial blocker during repositioning. Certainly 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. 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.

In addition, with the introduction of robotics for thoracic surgery careful attention must be given to airway devices because changes in patient position required for robotic surgery have the potential to cause malposition of airway devices. In robotic thoracic surgery access to the airway in midoperation can be very difficult.¹²⁷

Neurovascular Complications

There is a specific set of nerve and vascular injuries related to the lateral position that must be appreciated. The brachial plexus is the site of the majority of intraoperative nerve injuries related to the lateral position.¹²⁸ 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

BOX 53.9 Factors That Contribute to Brachial Plexus Injury in the Lateral Position

- a. Dependent arm (compression injuries)
 - 1. Arm directly under thorax
 - 2. Pressure on clavicle into retroclavicular space
 - 3. Cervical rib
 - 4. Caudal migration of thorax padding into the axilla*
- b. Nondependent arm (stretch injuries)
 - 1. Lateral flexion of cervical spine
 - 2. Excessive abduction of arm (>90 degrees)
 - 3. Semiprone or semisupine repositioning after arm fixed to a support

*Unfortunately, this padding under the thorax is misnamed an “axillary roll” in some institutions. This padding absolutely should NOT be placed in the axilla.

points: proximally by the transverse process 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 (Box 53.9). The patient should be positioned with padding under the dependent thorax to keep the weight of the upper body off the dependent arm brachial plexus. However, this padding will exacerbate the pressure on the brachial plexus if it migrates superiorly into the axilla.

The arms should not be abducted beyond 90 degrees and should not be extended posteriorly beyond the neutral position nor flexed anteriorly greater than 90 degrees. 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.¹²⁹ This causes a deep, poorly circumscribed pain of posterior and lateral aspects of the shoulder and may be responsible for some cases of postthoracotomy shoulder pain.

It is very easy, after repositioning the patient in the lateral decubitus 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 can be 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.

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. Other sites particularly liable for neurovascular injury in the lateral position are the dependent ear pinna and eye. A “head-to-toe” protocol to monitor for possible neurovascular injuries related to the lateral decubitus position is presented in Box 53.10.

BOX 53.10 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*: (i) brachial plexus, (ii) circulation
- 6. Dependent and nondependent suprascapular nerves
- 7. Nondependent leg sciatic nerve
- 8. Dependent leg: (i) peroneal nerve, (ii) circulation

*Neurovascular injuries of the nondependent arm are more likely to occur if the arm is suspended or held in an independently positioned arm rest.

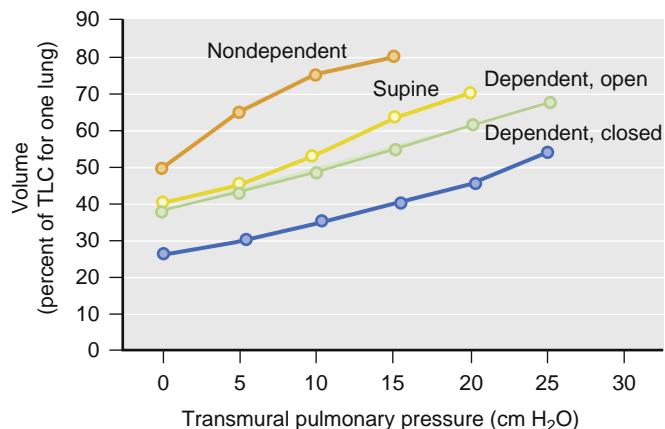


Fig. 53.27 Changes in the compliance of a single lung during position changes in an anesthetized, paralyzed patient during controlled mechanical ventilation. These compliance changes are responsible for the resulting differences in ventilation between the lungs that occur in the lateral position. Note: the compliance of the dependent lung is increased when the nondependent hemithorax is open versus closed. TLC, Total lung capacity.

Physiologic Changes in the Lateral Position

Ventilation. Significant changes in ventilation develop between the lungs when the patient is placed in the lateral position.¹³⁰ The compliance curves of the two lungs are different because of their difference in sizes. The lateral position, anesthesia, paralysis, and opening the thorax all combine to magnify these differences between the lungs (Fig. 53.27). The compliance curve (change in volume vs. change in pressure) of a lung depends on the balance of two “springs”: the chest wall (normally distending the lung) and the elastic recoil of the lung itself. Any factor that changes the mechanics of either of these springs places the lung on a different compliance curve.¹³¹

In a healthy, conscious, spontaneously breathing patient, the ventilation of the dependent lung will increase approximately 10% when the patient is turned to the lateral position. Once the patient is anesthetized and paralyzed, the ventilation of the dependent lung will then decrease 15%. Although the ventilation will not change significantly once the nondependent hemithorax is open, the FRC of this nondependent lung will tend to increase approximately 10%. These changes depend on the method used for ventilation in the individual patient.

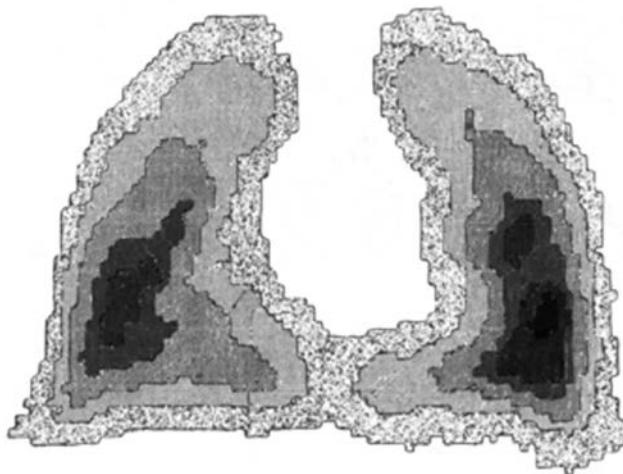


Fig. 53.28 In vivo perfusion lung scanning in the upright position demonstrates a predominant central to peripheral distribution of pulmonary blood flow in addition to a gravitational effect which also increases the blood flow in dependent lung regions. (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

When the chest is open, due to disruption of the chest wall, both lungs tend to collapse to a minimal lung volume if expiration is prolonged. Thus the end-expiratory volume of each lung is directly a function of the time allowed for expiration. The compliance of the entire respiratory system increases significantly once the non-dependent hemithorax is open.

Because of the fall in FRC and compliance of the dependent lung in the lateral position, application of PEEP selectively to this lung only (using a DLT and two anesthetic circuits), will improve gas exchange.¹³² This is different than the effect of nonselectively applying PEEP to both lungs in the lateral position where PEEP tends to preferentially distribute to the most compliant lung regions and will tend to hyperinflate the non-dependent lung without causing any improvement in gas exchange.¹³³

Atelectasis will develop in an average of 6% of the lung parenchyma after induction of anesthesia in the supine position. This atelectasis will be evenly distributed in the dependent portions of both lungs.¹³⁴ Turning the patient to the lateral position, there will be a slight decrease of total atelectasis to 5% of lung volume but this will now be concentrated totally in the dependent lung.

Perfusion. Gravity has some effect on distribution of pulmonary blood flow. In the lateral position, the blood flow to the dependent lung is generally thought to be increased by 10% compared to the same lung in the supine position.¹³⁵ However, the distribution of pulmonary blood flow in various positions may be more related to inherent pulmonary vascular anatomy than to gravity (Fig. 53.28).¹³⁶ The matching of ventilation and perfusion will usually be decreased in the lateral position compared to the supine position during anesthesia. Pulmonary arteriovenous shunt during general anesthesia will usually increase from approximately 5% in the supine position to 10% to 15% in the lateral position.¹³⁷

BOX 53.11 Fluid Management for Pulmonary Resection Surgery

- Total positive fluid balance in the first 24-h perioperative period should not exceed 20 mL/kg
- For an average adult patient, crystalloid administration should be limited to less than 3 L in the first 24 h
- No fluid administration for third-space fluid losses during pulmonary resection
- Urine output greater than 0.5 mL/kg/h is unnecessary
- If increased tissue perfusion is needed postoperatively, it is preferable to use invasive monitoring and inotropes rather than to cause fluid overload

Anesthetic Management

The development of thoracic anesthesia and thoracic surgery was delayed more than 50 years after the introduction of ether because anesthesiologists could not manage patients during mask anesthesia with spontaneous ventilation and an open chest. These patients developed what was originally called the “pneumothorax syndrome.”¹³⁸ The respiratory systems of mammals do not function adequately with an open hemithorax due to two physiologic problems. First, paradoxical ventilation (also called “pendelluft”) in which gas moves into the open-chest lung from the intact lung during expiration and then reverses flow during inspiration. This leads to hypercapnia and hypoxemia. And second, due to the swinging motion of the mediastinum between the hemithoraces during the respiratory cycle, which interferes with cardiac preload and causes hemodynamic instability. In the early 1900s, several pioneers such as the New Orleans surgeon Matas advocated positive-pressure ventilation and a primitive form of endotracheal ventilation, which had been demonstrated to be safe in animal experiments, for thoracic anesthesia. Modern methods, incorporating OLV, have evolved from this. Essentially any anesthetic technique that provides safe and stable general anesthesia for major surgery can and has been used for lung resection.

FLUID MANAGEMENT

Because of hydrostatic effects, excessive administration of intravenous fluids can cause increased shunting and subsequently lead to pulmonary edema of the dependent lung, particularly during prolonged surgery.¹³⁹ Because the dependent lung is the lung that must carry on gas exchange during OLV, it is best to be as judicious as possible with fluid administration. Intravenous fluids are administered to replace volume deficits and for maintenance only during lung resection anesthesia. No volume is given for theoretical “third space” losses (Box 53.11).¹⁴⁰

TEMPERATURE

Maintenance of body temperature can be a problem during thoracic surgery because of heat loss from the open hemithorax. This is particularly a problem at the extremes of the age spectrum. Most of the body’s physiological functions, including HPV, are inhibited during hypothermia.

Increasing the ambient room temperature, fluid warmers, and the use of lower and/or upper-body forced-air patient warmers are the best methods to prevent inadvertent intraoperative hypothermia.

PREVENTION OF BRONCHOSPASM

Because of the high incidence of coexisting reactive airways' disease in the thoracic surgical population, it is advisable to use an anesthetic technique that decreases bronchial irritability. This is particularly important because the added airway manipulation caused by placement of a DLT or bronchial blocker is a potent trigger for bronchoconstriction. The principles of anesthetic management are the same as they are for any asthmatic patient: avoid manipulation of the airway in a lightly anesthetized patient, use bronchodilating anesthetics, and avoid drugs that release histamine. For intravenous induction of anesthesia, either propofol or ketamine can be expected to diminish bronchospasm. This benefit is not seen with barbiturate, opioid, benzodiazepine, or etomidate intravenous induction. For maintenance of anesthesia, propofol and/or any of the volatile anesthetics will diminish bronchial reactivity. Sevoflurane may be the most potent bronchodilator of the volatile anesthetics.¹⁴¹

CORONARY ARTERY DISEASE

Because the lung resection population is largely elderly and smokers, there is a high coincidence of coronary artery disease. This consideration will be a major factor in the choice of the anesthetic technique for most thoracic patients. The anesthetic technique should optimize the myocardial oxygen supply/demand ratio by maintaining arterial oxygenation and diastolic blood pressure while avoiding unnecessary increases in cardiac output and heart rate. Thoracic epidural anesthesia/analgesia may aid in this (see Postoperative Analgesia later).

Management of One-Lung Ventilation

During OLV, the anesthesiologist has the unique and often conflicting goals of trying to maximize atelectasis in the nonventilated lung to improve surgical access while trying to avoid atelectasis in the ventilated lung (usually the dependent lung) to optimize gas exchange. The gas mixture in the nonventilated lung immediately before OLV has a significant effect on the speed of collapse of this lung. Because of its low blood-gas solubility, nitrogen (or an air-oxygen mixture) will delay collapse of this lung (Fig. 53.29).¹⁴² This is particularly a problem at the start of VATS surgery when surgical visualization in the operative hemithorax is limited and in patients with emphysema who have delayed collapse of the nonventilated lung because of decreased lung elastic recoil. It is important to thoroughly denitrogenate the operative lung, by ventilating with oxygen, immediately before it is allowed to collapse. Although nitrous oxide (N_2O) is even more effective than oxygen in speeding lung collapse, for the reasons just cited, it is not commonly used in thoracic anesthesia because many patients may have blebs or bullae.

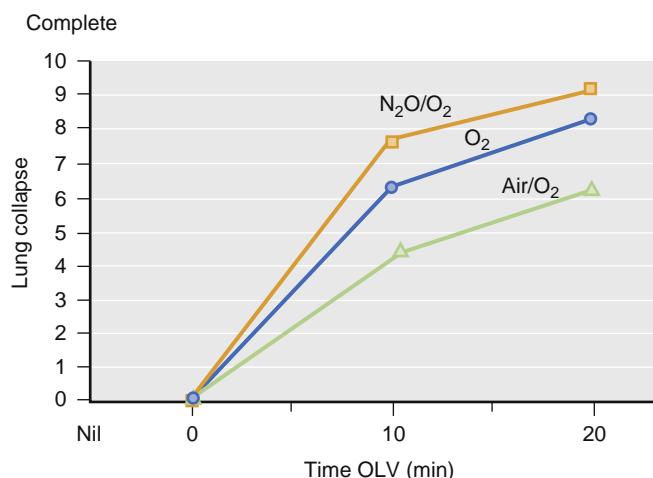


Fig. 53.29 The effects of the gas mixture used during two-lung ventilation (TLV), immediately before one-lung venation (OLV), on the speed of collapse of the nonventilated lung during OLV. $O_2 = FiO_2 1.0$; $N_2O/O_2 =$ nitrous oxide/oxygen 60/40; air/ $O_2 =$ air/oxygen $FiO_2 0.4$. All patients were ventilated with a FiO_2 of 1.0 during OLV. The poorly soluble nitrogen in the air/oxygen mixture delays collapse of the nonventilated lung. (Based on data from Ko R, et al. *Anesth Analg*. 2009;108:1029.)

Also, during the period of two-lung anesthesia before the start of OLV, atelectasis will develop in the dependent lung. It is useful to perform a recruitment maneuver to the dependent lung (similar to a Valsalva maneuver, holding the lung at an end-inspiratory pressure of 20 cm H₂O for 15–20 seconds) immediately after the start of OLV to decrease this atelectasis. Recruitment is important to maintain PaO_2 levels during subsequent OLV.¹⁴³

HYPOTENSION

A major concern that influences anesthetic management for thoracic surgery is the occurrence of hypoxemia during OLV. There is no universally acceptable figure for the safest lower limit of oxygen saturation during OLV. A saturation greater than or equal to 90% ($PaO_2 > 60$ mm Hg) is commonly accepted, and for brief periods a saturation in the high 80s may be acceptable in patients without significant comorbidity. However, the lowest acceptable saturation will be higher in patients with organs at risk of hypoxia because of limited regional blood flow (e.g., coronary or cerebrovascular disease) and in patients with limited oxygen transport (e.g., anemia or decreased cardiopulmonary reserve). It has been shown that during OLV patients with COPD desaturate more quickly during isovolemic hemodilution than normal patients.¹⁴⁴

Previously, hypoxemia occurred frequently during OLV. Reports for the period between 1950 and 1980 describe an incidence of hypoxemia (arterial saturation < 90%) of 20% to 25%.¹⁴⁵ More recent reports describe an incidence of less than 5%.¹⁴⁶ This improvement is most likely a result of several factors: improved lung isolation techniques such as routine fibroscopy to prevent lobar obstruction from DLTs, improved anesthetic drugs that cause less inhibition of HPV, and better understanding of the pathophysiology of OLV. The pathophysiology of OLV involves the body's ability to redistribute pulmonary blood flow to the ventilated lung. Several factors aid and impede this redistribution

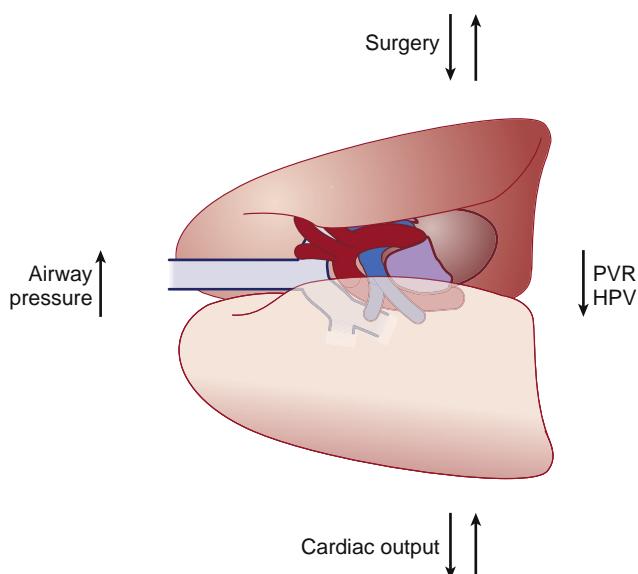


Fig. 53.30 Factors affecting the distribution of pulmonary blood flow during one-lung ventilation. Hypoxic pulmonary vasoconstriction (HPV), and the collapse of the nonventilated lung, which increases pulmonary vascular resistance (PVR), tend to distribute blood flow toward the ventilated lung. The airway pressure gradient between the ventilated and nonventilated thoraces tends to encourage blood flow to the nonventilated lung. Surgery and cardiac output can have variable effects, either increasing or decreasing the proportional flow to the ventilated lung.

and these are under the control of the anesthesiologist to a variable degree. These factors are illustrated in Fig. 53.30. The anesthesiologist's goal during OLV is to maximize PVR in the nonventilated lung while minimizing PVR in the ventilated lung. Key to understanding this physiology is the appreciation that PVR is correlated with lung volume in a hyperbolic fashion (Fig. 53.31). PVR is lowest at FRC and increases as lung volume rises or falls above or below FRC.¹⁴⁷ The anesthesiologist's aim, to optimize pulmonary blood flow redistribution during OLV, is to maintain the ventilated lung as close as possible to its FRC while facilitating collapse of the nonventilated lung to increase its PVR.

INTRAOPERATIVE POSITION

Most thoracic surgery is performed in the lateral position. Patients having OLV in the lateral position have significantly better PaO_2 levels than patients during OLV in the supine position.¹⁴⁸ This applies both to patients with normal lung function and to those with COPD (Fig. 53.32).¹⁴⁹

Hypoxic Pulmonary Vasoconstriction

HPV is thought to be able to decrease the blood flow to the nonventilated lung by 50%.¹⁵⁰ The stimulus for HPV is primarily the PAO_2 , which stimulates precapillary vasoconstriction, redistributing pulmonary blood flow away from hypoxic lung regions via a pathway involving NO and/or cyclooxygenase (COX) synthesis inhibition.¹⁵¹ The mixed venous PO_2 (P_vO_2) is also a stimulus although considerably weaker than PAO_2 . HPV has a biphasic temporal response

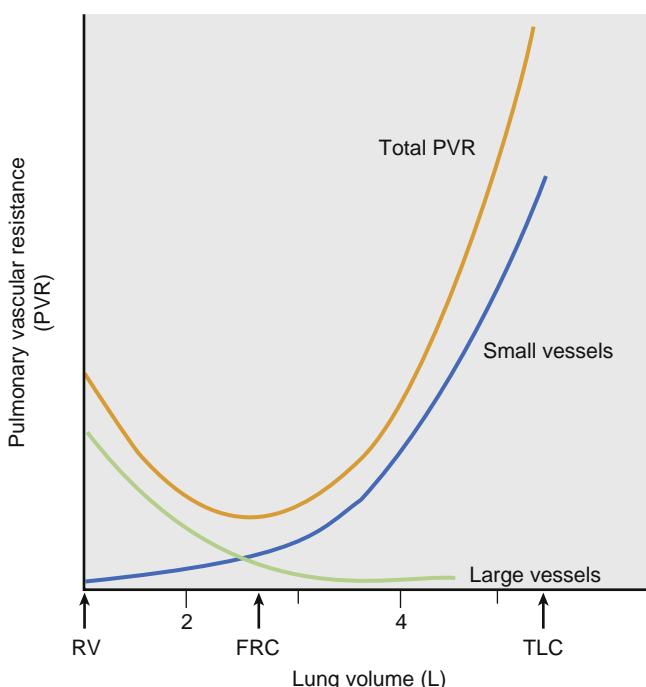


Fig. 53.31 The relationship between pulmonary vascular resistance (PVR) and lung volume. PVR is lowest at functional residual capacity (FRC) and increases as the lung volume decreases toward residual volume (RV), caused primarily by an increase in the resistance of large pulmonary vessels. PVR also increases as lung volume increases above FRC toward total lung capacity (TLC) as a result of an increase in the resistance of small interalveolar lung vessels.

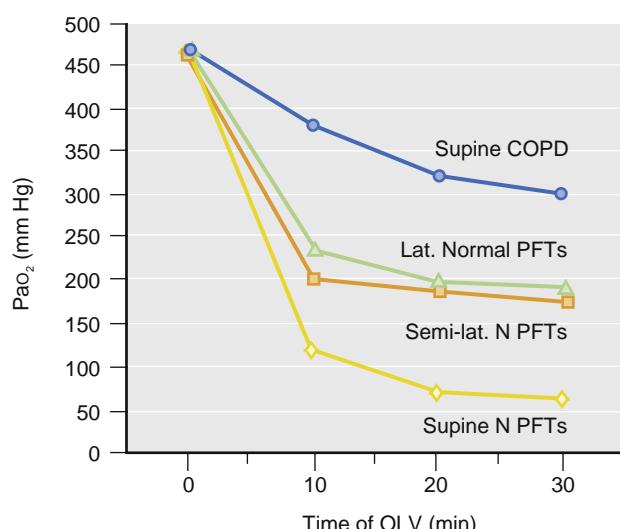


Fig. 53.32 Mean PaO_2 in groups of patients versus time of one-lung ventilation (OLV). Supine chronic obstructive pulmonary disease (COPD) = patients with COPD having OLV in the supine position. Lat. Normal PFTs = patients with normal pulmonary function having OLV in the lateral position. Semi-lat. N PFTs = patients with normal pulmonary function having OLV in the semilateral position. Supine N PFTs = patients with normal pulmonary function having OLV in the supine position. Patients with normal pulmonary function having OLV in the supine position are the most likely to desaturate. (Based on data from Watanabe S, et al. *Anesth Anal*. 2000;90:28; and Bardoczy G, et al. *Anesth Analg*. 2008;90:35.)

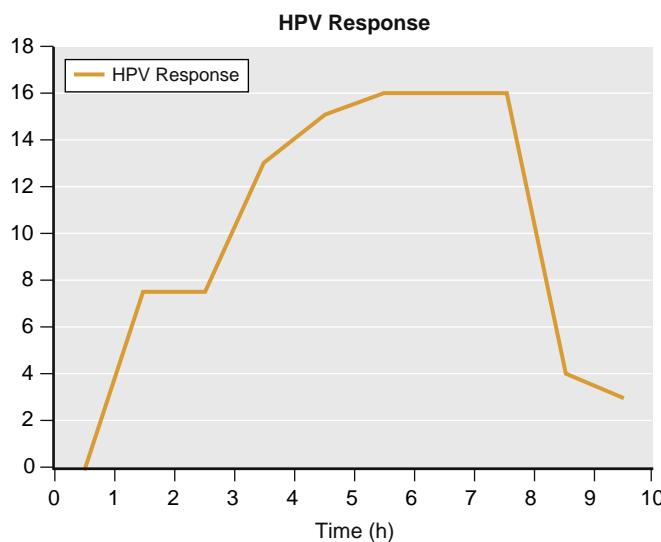


Fig. 53.33 The relationship between hypoxic pulmonary vasoconstriction (HPV) (vertical axis) and time in hours (h) (horizontal axis) in humans exposed to isocapnic hypoxia (approximate inspired PO_2 60 mm Hg) beginning at baseline with a return to normoxia at 8 hours. HPV response was measured as the increase in echocardiographic right ventricular systolic pressure. Note the two-phase, rapid and slow, onset of HPV. Also note that after prolonged HPV, the pulmonary pressures do not return to baseline for several hours. (Based on data from Talbot, et al. *J Appl Physiol*. 2005;98:1125.)

to alveolar hypoxia. The rapid-onset phase begins immediately and reaches a plateau by 20 to 30 minutes. The second (delayed) phase begins after 40 minutes and plateaus after 2 hours (Fig. 53.33).¹⁵² The offset of HPV is also biphasic and PVR may not return to baseline for several hours after a prolonged period of OLV. This may contribute to increased desaturation during the collapse of the second lung during bilateral thoracic procedures. HPV is also a reflex that has a preconditioning effect and the response to a second hypoxic challenge will be greater than to the first challenge.¹⁵³

The surgical trauma to the lung can affect pulmonary blood flow redistribution. Surgery may oppose HPV by release of vasoactive metabolites locally in the lung. Conversely, surgery can dramatically decrease blood flow to the nonventilated lung by deliberately or accidentally mechanically interfering with either the unilateral pulmonary arterial or venous blood flow.¹⁵⁴ Ventilation increases blood flow through a hypoxic lung more than in a normoxic lung, which is generally not of clinical relevance but does complicate studies of HPV. HPV is decreased by vasodilators such as nitroglycerin and nitroprusside. In general, vasodilators can be expected to cause a deterioration in P_{aO_2} during OLV. Thoracic epidural sympathetic blockade probably has little or no direct effect on HPV, which is a localized chemical response in the lung.¹⁵⁵ However thoracic epidural anesthesia can have an indirect effect on oxygenation during OLV if it is allowed to cause hypotension and a fall in cardiac output (see “Cardiac Output” later).

CHOICE OF ANESTHETIC

All of the volatile anesthetics inhibit HPV in a dose-dependent fashion. Animal studies suggest that this inhibition is dependent on the agent: halothane > enflurane >

isoflurane.¹⁵⁶ The older anesthetics were potent inhibitors of HPV and this may have contributed to the high incidence of hypoxemia reported during OLV in the 1960s and 1970s (see earlier); many of these studies used 2- to 3-minimum alveolar concentration (MAC) doses of halothane.

In doses of less than or equal to 1 MAC, the modern volatile anesthetics (isoflurane, sevoflurane,¹⁵⁷ and desflurane¹⁵⁸) are weak, and equipotent, inhibitors of HPV. The inhibition of the HPV response by 1 MAC of a volatile anesthetic such as isoflurane is approximately 20% of the total HPV response, and this could account for only a net 4% increase in total arteriovenous shunt during OLV, which is a difference too small to be detected in most clinical studies.¹⁵⁹ In addition, volatile anesthetics cause less inhibition of HPV when delivered to the active site of vasoconstriction via the pulmonary arterial blood than via the alveolus. This pattern is similar to the HPV stimulus characteristics of oxygen. During established OLV, the volatile agent only reaches the hypoxic lung pulmonary capillaries via the mixed venous blood. No clinical benefit in oxygenation during OLV has been shown for total intravenous anesthesia above that seen with 1 MAC of the modern volatile anesthetics.¹⁶⁰

The use of $\text{N}_2\text{O}/\text{O}_2$ mixtures is associated with a higher incidence of postthoracotomy radiographic atelectasis (51%) in the dependent lung than when air/oxygen mixtures are used (24%). N_2O also tends to increase pulmonary artery pressures in patients who have pulmonary hypertension and N_2O inhibits HPV. For these reasons N_2O is usually avoided during thoracic anesthesia.

Volatile anesthetic techniques seem to be associated with less release of proinflammatory cytokines and possibly fewer postoperative pulmonary complications following OLV compared to intravenous anesthetics. In a randomized study comparing sevoflurane to propofol for anesthesia in pulmonary resection, the sevoflurane group had significantly fewer postoperative pulmonary complications (14% vs. 28%) and lower 1-year mortality (2.3% vs. 12.5%).¹⁶¹

CARDIAC OUTPUT

The effects of alterations of cardiac output during OLV are complex (Fig. 53.34). Increasing cardiac output tends to cause increased pulmonary artery pressures and passive dilation of the pulmonary vascular bed, which in turn opposes HPV and has been shown to be associated with increased arteriovenous shunt (Q_s/Q_t) during OLV.¹⁶² However, in patients with a relatively fixed oxygen consumption, as is seen during stable anesthesia, the effect of an increase in cardiac output is to increase the SvO_2 . Thus increasing cardiac output during OLV tends to increase both shunt and SvO_2 , which have opposing effects on P_{aO_2} . There is a ceiling effect to the amount that SvO_2 can be increased. Increasing the cardiac output to supranormal levels by administering inotropes, such as dopamine, tends to have an overall negative effect on PaO_2 .¹⁶³ Conversely, allowing the cardiac output to fall will lead to falls in both shunt and SvO_2 with a net effect of decreasing PaO_2 . Because even with optimal anesthetic management there is usually a shunt of 20% to 30% during OLV, it is very important to maintain cardiac output.

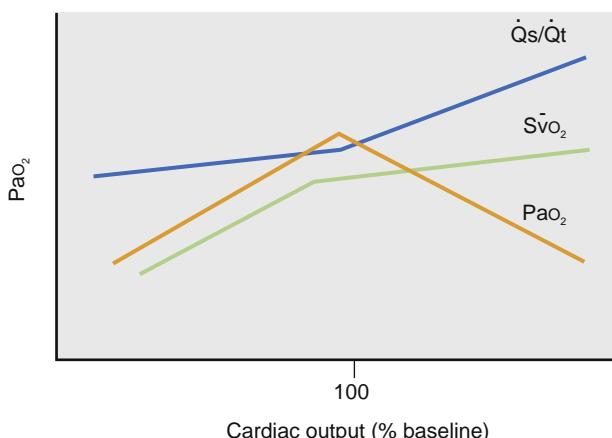


Fig. 53.34 The relationship between PaO_2 and cardiac output during OLV. As cardiac output falls below baseline, arteriovenous shunt (\dot{Q}_s/\dot{Q}_t) falls, but the mixed venous oxygen saturation (SvO_2) also decreases, resulting in a net fall in PaO_2 . Conversely, raising cardiac output above baseline tends to increase SvO_2 but also increase \dot{Q}_s/\dot{Q}_t and the net result again is a decrease in PaO_2 . OLV, One-lung ventilation. (Based on data from Slinger P, Scott W. *Anesthesiology*. 1995;82:940, and Russell W, James M. *Anaesth Intens Care*. 2004;32:644.)

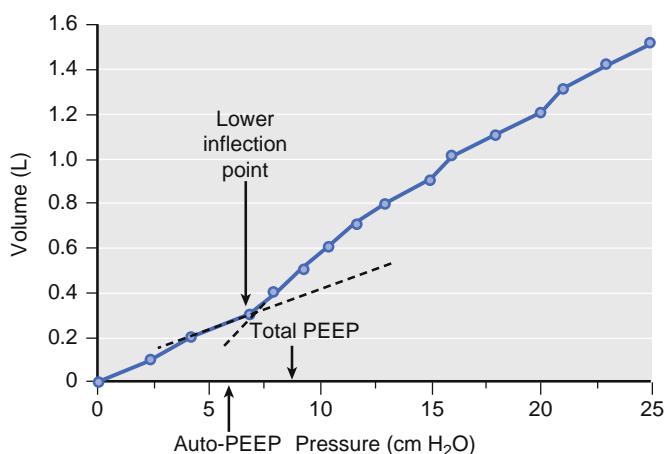


Fig. 53.35 The static compliance curve of the ventilated (dependent) lung in a typical lung cancer patient with mild COPD. The Lower Inflection Point is thought to represent functional residual capacity. This patient had 6 cm H_2O of auto-PEEP during OLV. Adding 5 cm H_2O PEEP to the ventilator resulted in a total PEEP in the circuit of 9 cm H_2O . This patient had a decrease in PaO_2 with the addition of PEEP. *auto-PEEP*, Occult positive end-expiratory pressure; *COPD*, chronic obstructive pulmonary disease; *PEEP*, positive end-expiratory pressure. (Based on data from Slinger P, et al. *Anesthesiology*. 2001;95:1096.)

Ventilation Strategies During One-Lung Ventilation

The strategy used to manage the ventilated lung during OLV plays an important part in the distribution of pulmonary blood flow between the lungs. It has been the practice of many anesthesiologists to use the same large tidal volume (e.g., 10 mL/kg ideal body weight) during OLV as during TLV. This strategy probably decreases hypoxemia by recurrently recruiting atelectatic regions in the dependent lung and may result in higher PaO_2 values during OLV than compared to smaller tidal volumes.¹⁶⁴ However, there is a trend to use smaller tidal volumes with PEEP during OLV for several reasons. First, the incidence of hypoxemia during OLV is much lower than 20 to 30 years ago. Second, there is a risk of causing acute injury to the ventilated lung with prolonged use of large tidal volumes. And third, a ventilation pattern that allows recurrent atelectasis and recruitment of lung parenchyma seems to be injurious.¹⁶⁵ The ventilation technique needs to be individualized depending on the patient's underlying lung mechanics.

RESPIRATORY ACID-BASE STATUS

The efficacy of HPV in a hypoxic lung region is increased in the presence of respiratory acidosis and is inhibited by respiratory alkalosis. However, there is no net benefit to gas exchange during OLV from hypoventilation because the respiratory acidosis preferentially increases the pulmonary vascular tone of the well-oxygenated lung and this opposes any clinically useful pulmonary blood flow redistribution.¹⁶⁶ Overall, the effects of hyperventilation will usually tend to decrease pulmonary vascular pressures.

POSITIVE END-EXPIRATORY PRESSURE

Resistance to blood flow through the lung is related to lung volume in a biphasic pattern and is lowest when the lung is

at its FRC. Keeping the ventilated lung as close as possible to its normal FRC favorably encourages pulmonary blood flow to this lung. Several intraoperative factors known to alter FRC tend to cause the FRC of the ventilated lung to fall below its normal level; these include lateral position, paralysis, and opening the nondependent hemithorax, which allows the weight of the mediastinum to compress the dependent lung. Attempts to measure FRC in human patients during OLV have been complicated by the presence of a persistent end-expiratory airflow in COPD patients.¹⁶⁷ Many patients do not actually reach their end-expiratory equilibrium FRC lung volume as they try to exhale a relatively large tidal volume through one lumen of a DLT. These patients develop dynamic hyperinflation and an occult positive end-expiratory pressure (auto-PEEP).⁶¹

Auto-PEEP occurs in patients with decreased lung elastic recoil, such as the elderly or those with emphysema.¹⁶⁸ Auto-PEEP increases as the inspiratory/expiratory (I:E) ratio increases (i.e., as the time of expiration decreases). This auto-PEEP, which averages 4 to 6 cm H_2O in most series of lung cancer patients with COPD, opposes the previously mentioned factors, which tend to diminish dependent-lung FRC during OLV. The effects of applying external PEEP through the ventilator circuit to the lung in the presence of auto-PEEP are complex (Fig. 53.35). Patients with low auto-PEEP (<2 cm H_2O) will experience a greater increase in total PEEP from a moderate (5 cm H_2O) external PEEP than those with a high level of auto PEEP (>10 cm H_2O). Whether the application of PEEP during OLV will improve a patient's gas exchange depends on the individual's lung mechanics. If the application of PEEP tends to shift the expiratory equilibration position on the compliance curve toward the lower inflection point (LIP) of the curve (i.e., toward the FRC) then external PEEP is of benefit (Fig. 53.36). However, if the application of PEEP raises the equilibration point such that it is further from the LIP, then gas exchange deteriorates.

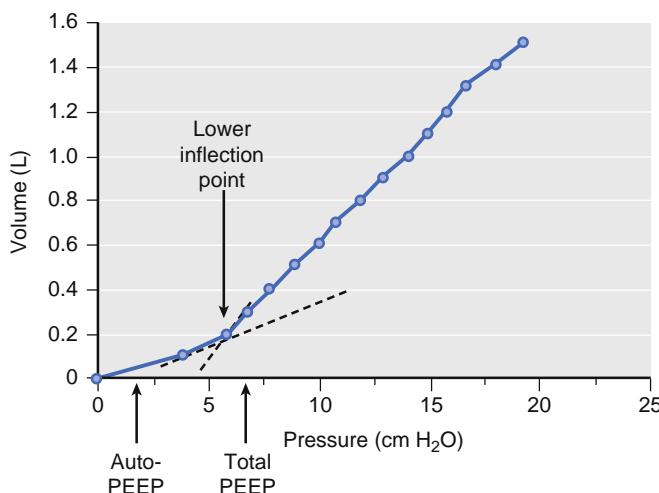


Fig. 53.36 Static compliance curve of a young patient with normal pulmonary function during OLV (in this case for removal of a mediastinal tumor). The Lower Inflection Point of the curve (functional residual capacity) was at 6 cm H₂O. The patient had 2 cm H₂O auto-PEEP during OLV. Adding 5 cm H₂O PEEP to the ventilator raised the total PEEP to 7 cm H₂O and improved PaO₂. Patients with normal lung mechanics and patients with increased lung elastic recoil (such as caused by restrictive lung diseases) have an increase in PaO₂ from PEEP during OLV. *auto-PEEP*, occult positive end-expiratory pressure; *OLV*, One-lung ventilation; *PEEP*, positive end-expiratory pressure. (Based on data from Slinger P, et al. *Anesthesiology*. 2001;95:1096.)

Auto-PEEP is difficult to detect and measure using currently available anesthetic ventilators. To detect auto-PEEP the respiratory circuit must be held closed at the end of a normal expiration until an equilibrium appears in the airway pressure.¹⁶⁹ Most current intensive care ventilators can be used to measure auto-PEEP.

TIDAL VOLUME

There will be an optimal combination of tidal volume, respiratory rate, I:E ratio, and pressure- or volume-control ventilation for each individual patient during OLV. However, to try to assess each of these parameters while still providing anesthesia with the available anesthetic ventilators is not practical, and the clinician must initially rely on a simplified strategy (Table 53.9). The results of alterations in tidal volume are unpredictable. This may be caused partly by the interaction of tidal volume with auto-PEEP. The use of 5 to 6 mL/kg ideal body weight tidal volumes plus 5 cm H₂O PEEP initially for most patients (except those with COPD) seems a logical starting point during OLV.¹⁷⁰ Tidal volume should be managed so that peak airway pressures do not exceed 35 cm H₂O. This will correspond to a plateau airway pressure of approximately 25 cm H₂O.¹⁷¹ Peak airway pressures exceeding 40 cm H₂O may contribute to hyperinflation injury of the ventilated lung during OLV.¹⁷²

Turning the patient to the lateral position will increase respiratory dead space and the arterial to end-tidal CO₂ tension gradient (P_{a-ET}CO₂). This will usually require a 20% increase in minute ventilation to maintain the same P_aCO₂. Individual variations in P_{a-ET}CO₂ gradient become much larger, and P_{ET}CO₂ is less reliable as a monitor of P_aCO₂ during OLV. This effect is possibly because there are individual differences in the excretion of CO₂ between the dependent and nondependent lungs.

TABLE 53.9 Suggested Ventilation Parameters for One-Lung Ventilation

Parameter	Suggested	Guidelines/Exceptions
1. Tidal volume	5–6 mL/kg ideal body weight	Maintain: Peak airway pressure <35 cm H ₂ O Plateau airway pressure <25 cm H ₂ O
2. Positive end-expiratory pressure	5–10 cm H ₂ O	Patients with COPD, no added PEEP
3. Respiratory rate	12 breaths/min	Maintain normal PaCO ₂ . Pa-ET CO ₂ will usually increase 1–3 mm Hg during OLV
4. Mode	Pressure-controlled or volume-controlled	Pressure-control for patients at risk of lung injury (e.g., bullae, pneumonectomy, postlung transplantation)

COPD, Chronic obstructive pulmonary disease; OLV, one-lung ventilation; PEEP, positive end-expiratory pressure.

VOLUME-CONTROL VERSUS PRESSURE-CONTROL VENTILATION

Pressure-control ventilation has not been shown to improve oxygenation versus volume-control ventilation for most patients, although the peak airway pressures are lower.¹⁷³ The decrease in peak pressure with pressure-control ventilation may be largely in the anesthetic circuit and not at the distal airway.¹⁷⁴ Pressure-control ventilation will avoid sudden increases in peak airway pressures that may result from surgical manipulation in the chest. This will be of benefit when a bronchial blocker is used and in patients at increased risk for lung injury from high pressures such as after lung transplantation or during a pneumonectomy.¹⁷⁵ Because of the rapid changes of lung compliance that occur during pulmonary surgery, when pressure-control ventilation is used the delivered tidal volume needs to be closely monitored as this may change suddenly.

Prediction of Hypoxemia During One-Lung Ventilation

The problem of hypoxemia during OLV has prompted much research in thoracic anesthesia. Hypoxemia during OLV is predictable (see Box 53.7), preventable, and treatable in the vast majority of cases.¹⁷⁶

PREOPERATIVE VENTILATION-PERFUSION SCAN

The shunt and P_aO₂ during intraoperative OLV are highly correlated with the fractional perfusion of the ventilated lung as determined by a preoperative ventilation/perfusion scan.¹⁷⁷ Patients with long-standing unilateral disease on the operative side develop a unilateral decrease of ventilation and perfusion and tolerate OLV very well. Similarly, patients who intraoperatively have a higher proportion of gas exchange in the dependent lung during OLV tend to have better oxygenation during OLV.

SIDE OF OPERATION

Patients having right-sided thoracotomies tend to have a larger shunt and lower P_aO_2 during OLV because the right lung is larger and normally 10% better perfused than the left. The overall mean P_aO_2 difference between left and right thoracotomies during stable OLV is approximately 100 mm Hg.¹⁷⁸

TWO-LUNG OXYGENATION

Patients who have better P_aO_2 levels during TLV in the lateral position tend to have better oxygenation during OLV. These patients may have better abilities to match ventilation and perfusion (individual variability of HPV response) and/or they may have less atelectasis in the dependent lung. This is a particularly relevant consideration in trauma patients who may require a thoracotomy but have a contusion of the dependent lung.

PREOPERATIVE SPIROMETRY

Studies consistently show that when the aforementioned factors are controlled, patients with better spirometric lung function preoperatively are more likely to desaturate and have lower P_aO_2 values during OLV. Clinically this is evident because emphysematous lung-volume reduction patients generally tolerate OLV very well. The explanation is not clear but may be related to maintenance of a more favorable FRC in patients with obstructive airways' disease during OLV with an open hemithorax due to the development of auto-PEEP.⁶⁴

Treatment of Hypoxemia During One-Lung Ventilation

During OLV there will be a fall in arterial oxygenation that usually reaches its nadir 20 to 30 minutes after the initiation of OLV then the saturation will stabilize or may rise slightly as HPV increases over the next 2 hours. The majority of patients who desaturate do so quickly and within the first 10 minutes of OLV. Hypoxemia during OLV responds readily to treatment in the vast majority of cases. Potential therapies are outlined in [Box 53.12](#).

1. Resume two-lung ventilation. Reinflate the nonventilated lung and deflate the bronchial cuff of the DLT or the bronchial blocker. This will necessitate interruption of surgery but is necessary in case of severe or precipitate desaturation. After an adequate level of oxygenation is obtained, the diagnosis of the cause of desaturation can be made and prophylactic measures instituted (see later) before another trial of OLV is attempted.
2. Increase FiO_2 . Ensure that the delivered FiO_2 is 1.0. This is an option in essentially all patients except those who have received bleomycin or similar therapies that potentiate pulmonary oxygen toxicity.
3. Recheck the position of the DLT or bronchial blocker. Ensure that there is no lobar obstruction in the ventilated lung.
4. Check the patient's hemodynamics to ensure that there has been no decrease in cardiac output. It is very com-

BOX 53.12 Therapies for Desaturation during One-Lung Ventilation

- **Severe or precipitous desaturation:** resume two-lung ventilation (if possible)
- **Gradual desaturation:**
 - Ensure that delivered FiO_2 is 1.0
 - Check position of double-lumen tube or blocker with fiberoptic bronchoscopy
 - Ensure that cardiac output is optimal, decrease volatile anesthetics to <1 MAC
 - Apply a recruitment maneuver to the ventilated lung (this will transiently make the hypoxemia worse)
 - Increase PEEP to the ventilated lung (except in patients with emphysematous pathology)
 - Apneic oxygen insufflation of the nonventilated lung
 - Apply CPAP 1–2 cm H_2O to the nonventilated lung (apply a recruitment maneuver to this lung immediately before CPAP)
 - Partial ventilation techniques of the nonventilated lung
 - Intermittent positive pressure ventilation
 - Fiberoptic lobar insufflation
 - Selective lobar collapse (using a bronchial blocker)
 - Small tidal volume ventilation
 - Pharmacologic manipulations (see text)
 - Mechanical restriction of the blood flow to the nonventilated lung (if possible)
 - Venovenous ECMO

CPAP, Continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; MAC, minimum alveolar concentration; PEEP, positive end-expiratory pressure.

mon for the surgeon to accidentally compress the inferior vena cava during pulmonary resections and the fall in blood pressure and cardiac output that this causes leads to rapid desaturation during OLV. Treat the fall in cardiac output as indicated (e.g., inotropes/vasopressors if due to thoracic epidural sympathetic blockade). Stop administration of vasodilators, decrease MAC of volatile anesthetics to less than or equal to 1 MAC.

5. Perform a recruitment maneuver of the ventilated lung. To eliminate any atelectasis inflate the lung to 20 cm H_2O or more for 15 to 20 seconds. This may cause transient hypotension and will also cause a transient further fall in the PaO_2 as the blood flow is temporarily redistributed to the nonventilated lung.
6. Apply PEEP to the ventilated lung. It is necessary to perform a recruitment maneuver before applying PEEP to get the maximal benefit. PEEP will raise the end-expiratory volume of the ventilated lung toward the FRC in patients with normal lung mechanics and in those with increased elastic recoil caused by restrictive disease. It is not possible to predict the optimal PEEP for individual patients. It is useful to titrate PEEP between 5 to 10 cm H_2O to maximize compliance while maintaining a driving pressure (plateau pressure-PEEP) of 15 cm H_2O or less.¹⁷⁹ PEEP will increase the end-expiratory lung volume of patients with significant levels of auto-PEEP (e.g., emphysema patients). Unlike CPAP, application of PEEP does not require reinflation of the nonventilated lung and interruption of surgery. PEEP has been shown to be as effective for increasing PaO_2 levels during OLV in patients with normal lung function as CPAP

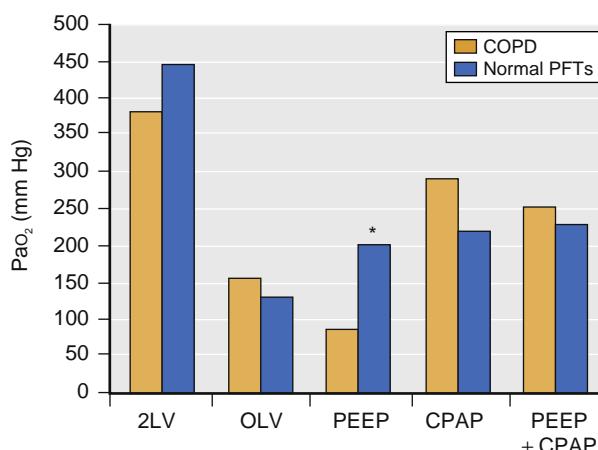


Fig. 53.37 A comparison of the effects of positive end-expiratory pressure (PEEP) to the ventilated lung and continuous positive airway pressure (CPAP) to the nonventilated lung on mean PaO_2 levels during one-lung ventilation (OLV). 2LV, Two-lung ventilation; COPD, a group of lung cancer surgery patients; Normal PFTs, a group of esophageal surgery patients with normal preoperative pulmonary function tests.

*Significance of $P < .05$ versus OLV. (Based on data from Fujiwara M, et al. *J Clin Anesth*. 2001;13:473; and Capan L, et al. *Anesth Analg*. 1980;59:847.)

(Fig. 53.37).¹⁸⁰ For patients with normal pulmonary function it is logical to routinely apply a recruitment maneuver and PEEP from the start of OLV.

7. Apneic oxygen insufflation to the nondependent lung. Application of 3 liters of O_2 , via a suction catheter to the nonventilated lumen of the DLT, improved PaO_2 during OLV without interference to the surgical field.¹⁸¹
8. CPAP with oxygen to the nonventilated lung is a reliable method to improve PaO_2 during OLV.¹⁸² CPAP should be applied to an inflated (recruited) lung to be completely effective. The opening pressure of atelectatic lung regions is greater than 20 $\text{cm H}_2\text{O}$ ¹⁸³ and these units will not be recruited by simple application of CPAP levels of 5 to 10 $\text{cm H}_2\text{O}$.¹⁸⁴ When CPAP is applied to an inflated lung, levels of CPAP as low as 1 to 2 $\text{cm H}_2\text{O}$ can be used.¹⁸⁵ Since the normal transpulmonary pressure of the lung at FRC is approximately 5 $\text{cm H}_2\text{O}$, levels of 5 to 10 $\text{cm H}_2\text{O}$ CPAP applied to a fully recruited lung result in a large-volume lung that impedes surgery particularly during minimally invasive procedures. Lower FiO_2 levels of CPAP are of clinical benefit and can be titrated to the ventilated lung in patients at risk of oxygen toxicity using an air/oxygen blender.

Numerous anesthetic systems to apply CPAP to the nonventilated lung have been described. Essentially all that is required is a CPAP (or PEEP) valve and an oxygen source. Ideally the circuit should permit variation of the CPAP level and include a reservoir bag to allow easy reinflation of the nonventilated lung and a manometer to measure the actual CPAP supplied. Such circuits are commercially available (Fig. 53.38) or can be readily constructed from standard anesthetic equipment.

CPAP, even when properly administered, is not completely reliable to improve oxygenation during OLV. When the bronchus of the operative lung is obstructed, or open to atmosphere (as in a bronchopleural fistula or during endobronchial surgery), CPAP will not improve oxygenation. Also in certain situations, particularly during thoracoscopic



Fig. 53.38 Photograph of a commercial (Mallinckrodt, St. Louis, MO) disposable CPAP circuit applied to the nonventilated lung during a left thoracotomy (in this case applied to the tracheal lumen of a right-sided DLT). This circuit has an adjustable exhaust valve that allows titration of CPAP between 1 and 10 $\text{cm H}_2\text{O}$. CPAP, Continuous positive airway pressure; DLT, double-lumen endobronchial tube.

surgery where access to the operative hemithorax is limited, CPAP can significantly interfere with surgery.¹⁸⁶

9. Use of extracorporeal membrane oxygenation (ECMO). There have been multiple case reports of ECMO being used to manage thoracic surgery where oxygenation cannot be maintained with conventional techniques. The safety of venovenous ECMO makes it an option in some cases of complex lung surgery.¹⁸⁷

PHARMACOLOGIC MANIPULATIONS

Eliminating known potent vasodilators such as nitroglycerin, halothane, and large doses of other volatile anesthetics will improve oxygenation during OLV.¹⁸⁸ The combination of NO and other pulmonary vasoconstrictors such as phenylephrine has been shown to improve oxygenation in ventilated intensive care unit patients with adult respiratory distress syndrome¹⁸⁹ and this may have applications in OLV. Systemic administration of a vasoconstrictor, to enhance pulmonary vasoconstriction, with simultaneous administration of an inhaled pulmonary vasodilator to the ventilated lung may improve hypoxemia in some cases of desaturation during OLV. This has been reported with the combination of intravenous phenylephrine and inhaled epoprostenol (Flolan).¹⁹⁰ A caveat is that the glycine diluent for nebulized epoprostenol tends to build up in the heat-moisture exchange (HME) filter of an anesthetic circuit causing increased airflow resistance. The HME filter should be changed every hour when nebulized epoprostenol is used.

Another drug that has been used is dexmedetomidine, a selective α -2 adrenoreceptor agonist. One study has shown that a continuous infusion of dexmedetomidine during OLV with sevoflurane anesthesia improved oxygenation and increased the $\text{PaO}_2/\text{FiO}_2$ ratio during the intraoperative period.¹⁹¹ A subsequent meta-analysis reported that the use of dexmedetomidine improved the oxygenation index (assessment of intrapulmonary shunt and mean airway pressure) by improving oxygenation and decreasing intrapulmonary shunt fraction during OLV in patients receiving

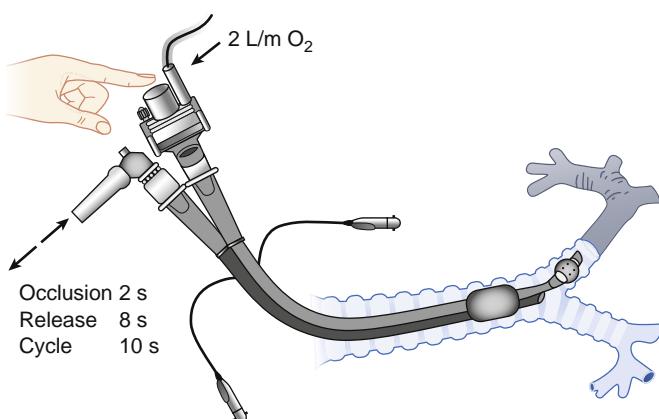


Fig. 53.39 A simple device to provide intermittent positive airway pressure to the nonventilated lung. A standard bacteriostatic filter is attached the lumen of the double-lumen tube to the nonventilated lung and an oxygen source is connected to the CO_2 sampling port of the filter. Intermittent manual occlusion of the open filter end improves oxygenation with minimal impact on surgical exposure (see text for details). (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

intravenous and or inhalational agents.¹⁹² One potential explanation for the effects of dexmedetomidine is that it reduces the required doses of inhalational anesthetics, thus reducing their potential negative effects on HPV.

INTERMITTENT REINFLATION OF THE NONVENTILATED LUNG

HPV becomes more effective during repeated hypoxic exposure. Often after reinflation, the oxygen saturation will be more acceptable during a second period of lung collapse. Reexpansion can be performed by regular reinflation of the operative lung via an attached CPAP circuit.

PARTIAL VENTILATION METHODS

Several alternative methods of OLV, all involving partial ventilation of the nonventilated lung, have been described and improve oxygenation during OLV. These techniques are useful in patients who are particularly at risk of desaturation such as those who have had previous pulmonary resections of the contralateral lung. These alternatives include:

1. Intermittent positive airway pressure to the nonventilated lung. This can be performed by a variety of methods. Russell described attaching a standard bacteriostatic filter to the nonventilated lumen of the DLT with a 2-L oxygen inflow attached to the CO_2 port of the filter (Fig. 53.39).¹⁹³ Manual occlusion of the filter for 2 seconds gives an insufflation of approximately 66 mL of oxygen to the nonventilated lung. This could be repeated at 10 second intervals with minimal interference with surgical exposure.
2. Selective insufflation of oxygen to recruit lung segments on the side of surgery but remote from the site of surgery (Fig. 53.40).¹⁹⁴ A useful technique in minimally invasive surgery is intermittent insufflation of oxygen using a fiberoptic bronchoscope. A 5-L oxygen flow is attached

to the suction port of a fiberoptic bronchoscope that is passed under direct vision into a segment of the lung remote from the site of surgery, which is then reinflated by triggering the suction on the fiberoptic bronchoscope. The surgeon aids this technique by observing the lung inflation with the videoscope to avoid overdistention of the recruited segment(s).

3. Selective lobar collapse of only the operative lobe in the open hemithorax.¹⁹⁵ This is accomplished by placement of a blocker in the appropriate lobar bronchus of the ipsilateral operative lung while continuing to ventilate the other lobe(s) of the lung.
4. Ventilation of the operative (nondependent lung) with a small tidal volume via another ventilator connected to a limb of a DLT to the nondependent lung. A brief period of intermittent positive pressure ventilation to the nondependent lung with a small tidal volume (e.g., 70 mL) and respiratory rate of 6/min was effective in improving PaO_2 and SpO_2 during OLV without interference with the surgery.¹⁹⁶

MECHANICAL RESTRICTION OF PULMONARY BLOOD FLOW

It is possible for the surgeon to directly compress or clamp the blood flow to the nonventilated lung.¹⁹⁷ This can be done temporarily in emergency desaturation situations or definitively in cases of pneumonectomy or lung transplantation. Another technique of mechanical limitation of blood flow to the nonventilated lung is the inflation of a pulmonary artery catheter balloon in the main pulmonary artery of the operative lung. The pulmonary artery catheter can be positioned at induction with fluoroscopic guidance and inflated as needed intraoperatively. This has been shown to be a useful technique for resection of large pulmonary arteriovenous fistulae.¹⁹⁸

HYPOXEMIA PROPHYLAXIS

The majority of the treatments outlined as therapies for hypoxemia can be used prophylactically to prevent hypoxemia in patients who are at high risk of desaturation during OLV. The advantage of prophylactic therapy of hypoxemia, in addition to the obvious patient safety benefit, is that maneuvers involving CPAP or alternative ventilation patterns of the operative lung can be instituted at the onset of OLV in a controlled fashion and will not require interruption of surgery and emergent reinflation of the nonventilated lung at a time that may be extremely disadvantageous.

BILATERAL PULMONARY SURGERY

Because of mechanical trauma to the operative lung, the gas exchange in this lung will always be temporarily impaired after OLV. Also HPV offset may be delayed after reinflation of the first lung collapsed. Desaturation during bilateral lung procedures is particularly a problem during the second period of OLV (i.e., during OLV of the lung that has already had surgery).¹⁹⁹ Thus for bilateral procedures it is advisable to operate first on the lung that has better gas exchange and less propensity to desaturate during OLV. For the majority of patients, this means operating on the right side first.

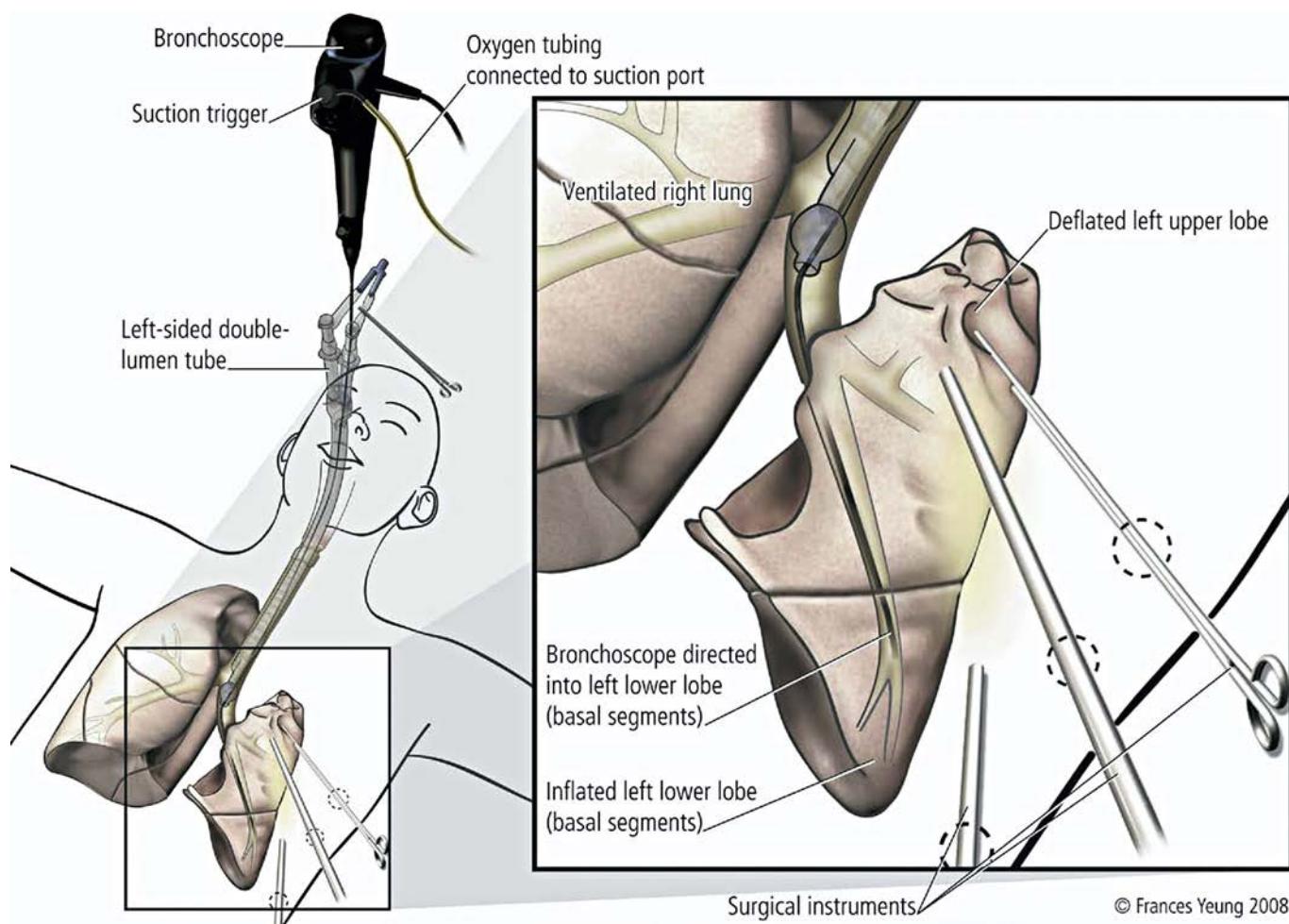


Fig. 53.40 Intermittent oxygen insufflation during thoracoscopic surgery to segments of the nonventilated lung on the side of surgery using a fiber-optic bronchoscope (see text for details). (Reproduced with permission from Slinger P. *Principles and Practice of Anesthesia for Thoracic Surgery*. New York: Springer; 2011.)

Anesthetic Management for Common Surgical Procedures

FLEXIBLE FIBEROPTIC BRONCHOSCOPY

Flexible fiberoptic bronchoscopy is a diagnostic and therapeutic procedure of great value in the clinical practice of thoracic surgery and anesthesia. In many centers, it is common practice to perform flexible fiberoptic bronchoscopy prior to lung resections, to reconfirm the diagnosis (if a tumor compresses the airway), or to determine the invasion and obstruction of the distal airway (in relation to the extension of the bronchial resection).

Anesthetic Management

There are multiple techniques for flexible fiberoptic bronchoscopy. Options include awake versus general anesthesia and oral versus nasal approaches. Options for local anesthesia include: topical anesthesia via a nebulizer, handheld aerosol, or soaked pledges; nerve blocks (laryngeal and/or glossopharyngeal nerves); direct administration of local anesthetic through the bronchoscope (spray-as-you-go technique),²⁰⁰ with/without sedation/opioid; or

antisialagogues. Options during general anesthesia include spontaneous versus positive-pressure ventilation with/without muscle relaxation. Airway management during general anesthesia can be with an ETT or a laryngeal mask airway (LMA). A Portex swivel connector with a self-sealing valve is used to facilitate the ventilation and manipulation of the bronchoscope; at the same time inhalation and/or intravenous agents can be used for anesthesia. Patients who have copious secretions in the preoperative period should receive anticholinergic medication to ensure a dry field, which provides optimal visualization with the flexible bronchoscope.

The advantages of an LMA technique include visualization of the vocal cords and subglottic structures as well as a lower airway resistance versus the ETT when the bronchoscope is inserted (Fig. 53.41). This is particularly useful in the patient with a difficult airway, when maintaining spontaneous respiration may be the safest method of anesthetic management.²⁰¹ Self-expanding flexometallic tracheal and bronchial stents can be placed with fiberoptic or rigid bronchoscopy (Fig. 53.42). However, Silastic airway stents require rigid bronchoscopy for placement.

RIGID BRONCHOSCOPY

Rigid bronchoscopy has traditionally been considered the technique of choice for the preoperative diagnostic assessment of an airway obstruction involving the trachea, and in the therapy of massive hemoptysis and foreign bodies in the airway. The role of interventional bronchoscopy with laser, bronchial dilation, or stent insertion is well established for the treatment of malignant and benign central airway and endobronchial lesions (Fig. 53.43).²⁰² Rigid bronchoscopy is the procedure of choice for operative procedures such as dilation of tracheal stenosis.

Anesthetic Management

Patients undergoing rigid bronchoscopy should have a complete preoperative evaluation including radiological studies. Chest radiographs and chest CT scans should be

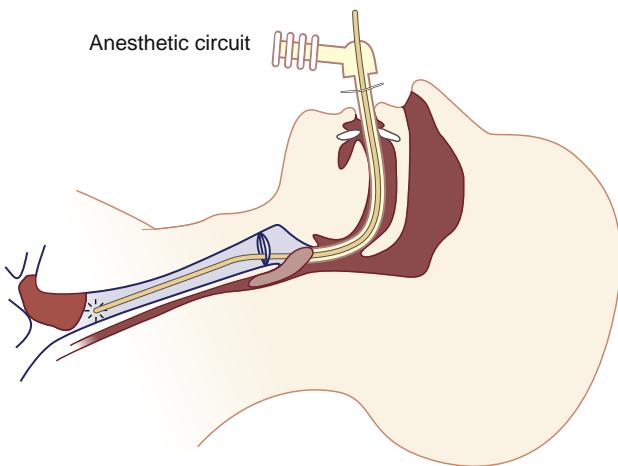


Fig. 53.41 Diagram of fiberoptic bronchoscopy performed via a laryngeal mask airway (LMA) during general anesthesia in a spontaneously breathing patient with a carinal tumor, in this case for diagnosis and Nd:YAG laser tumor excision. The LMA permits visualization of the vocal cords and subglottic structures with the bronchoscope, which is not possible when fiberoptic bronchoscopy is performed via an endotracheal tube.

reviewed in the preoperative evaluation. If time permits, it is recommended that patients with severe stridor receive pharmacologic interventions for temporary stabilization of the condition. Treatments may include inspired cool saline mist, nebulized racemic epinephrine, and the use of systemic steroids.²⁰³

There are four basic methods of ventilation management for rigid bronchoscopy:

1. Spontaneous ventilation. The addition of topical anesthesia or nerve blocks to the airway decreases the tendency to breath-hold and cough when volatile anesthetics are used.
2. Apneic oxygenation (with/without insufflation of oxygen). This requires thorough preoxygenation, and the anesthesiologist will have to interrupt surgery to ventilate the patient before desaturation occurs. This should allow the surgeon working intervals of 3 minutes or longer depending on the underlying condition of the patient.
3. Positive-pressure ventilation via a ventilating bronchoscope (Fig. 53.44). This allows the use of a standard anesthetic circuit but may cause significant air leaks if there is a discrepancy between the size of a smaller bronchoscope and a larger airway.
4. Jet ventilation. This can be performed with a handheld injector such as the Sanders injector²⁰⁴ or with a high-frequency ventilator. These techniques are most useful with intravenous anesthesia since they entrain gas from either the room air or an attached anesthetic circuit, and the dose of any volatile agent delivered will be very uncertain.

The use of anticholinergic agents (e.g., 0.2 mg intravenous glycopyrrolate) before manipulation of the airway will decrease secretions during the bronchoscopic examination. For a patient undergoing rigid bronchoscopy, the surgeon must be at the bedside for the induction of anesthesia and be prepared to establish airway control with the rigid bronchoscope. In children, anesthesia for rigid bronchoscopy is most commonly performed with spontaneous ventilation. In adults, intravenous anesthesia and the use of muscle relaxants is more common.

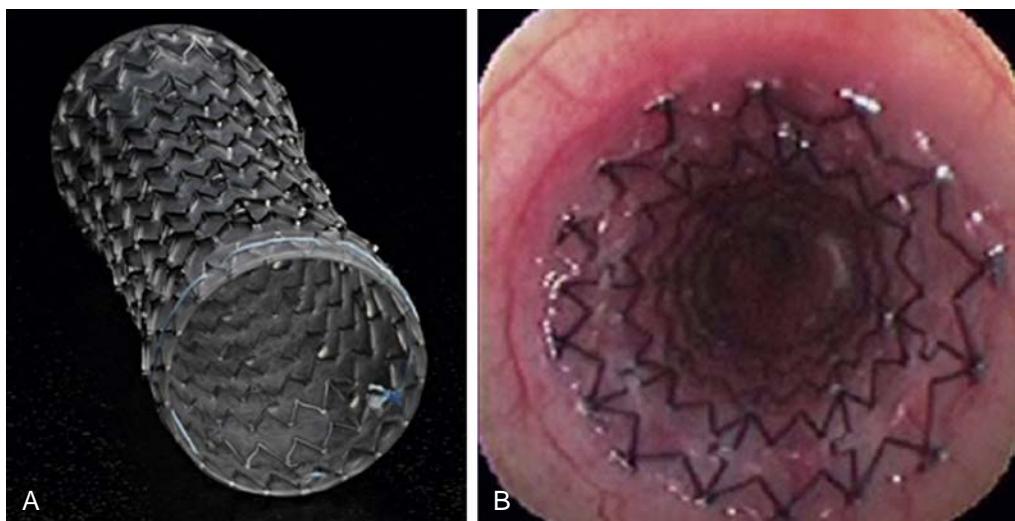


Fig. 53.42 (A) A self-expanding flexometallic airway stent. (B) Fiberoptic bronchoscopic view of the proximal end of a flexometallic tracheal stent.

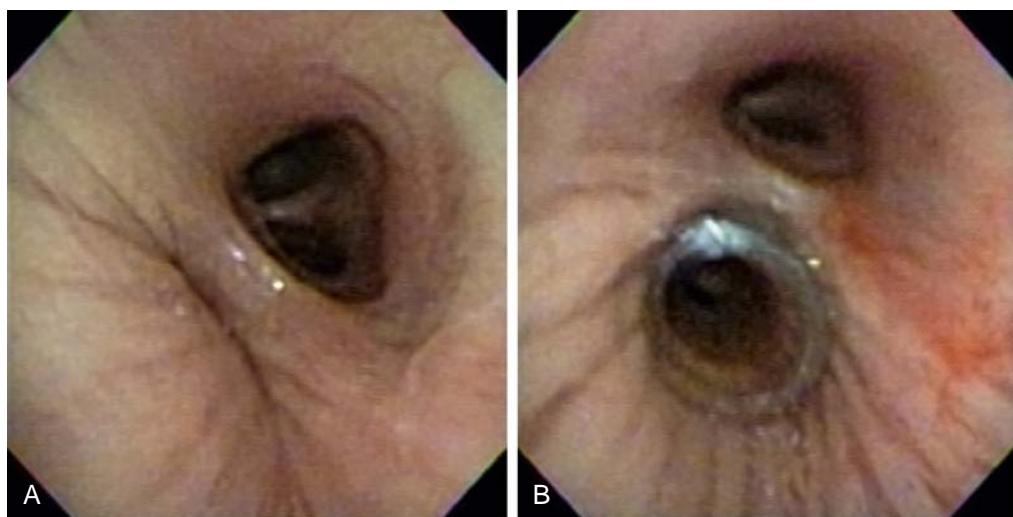


Fig. 53.43 (A) Photograph of a patient with a collapse of the left lower lobe bronchus post–lung transplantation. (B) A silastic stent has been placed in the left lower lobe bronchus with rigid bronchoscopy.

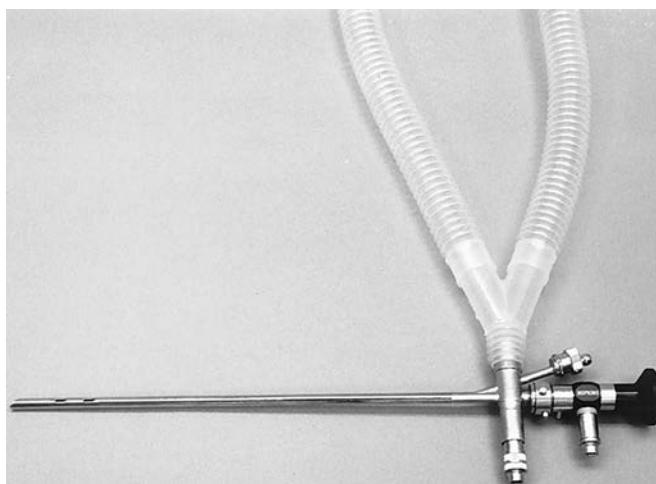


Fig. 53.44 Photograph of a ventilating rigid bronchoscope with an anesthetic circuit attached to the side arm. In this photograph there is a telescopic lens sealing the proximal end of the bronchoscope. (From Kaplan J, Slinger P, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003.)

In cases for which the use of muscle relaxants is not contraindicated, a short-acting agent (succinylcholine) can be used initially to facilitate intubation with either a small SLT or the rigid bronchoscope. Nondepolarizing relaxants may be needed for prolonged procedures such as stent placement or tumor resection. Mouth guards should be used to protect the upper and lower teeth and gums from the pressure of the bronchoscope. Remifentanil and propofol infusions can be administered if an intravenous regimen is the planned anesthetic.²⁰⁵ This is a useful technique if the surgeon needs repeated access (for suction or instrumentation) to the open airway since it maintains the level of anesthesia and avoids contaminating the operating room with exhaled anesthetic vapors.

For cases in which a neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser is used, the FiO_2 should be maintained in the lowest acceptable range (i.e., <30% if possible) according to patient oxygen saturation, to avoid the potential for fire in the airway. Since any common

material (including porcelain and metal) can be perforated by the Nd:YAG laser it is best to avoid any potentially combustible substance in the airway when the Nd:YAG laser is used.²⁰⁶ Because of its high energy and short wavelength, the Nd:YAG laser has several advantages for distal airway surgery over the CO_2 -laser, which is used in upper airway surgery. The Nd:YAG laser penetrates tissue more deeply so it causes more coagulation in vascular tumors and it can be refracted and passed in fibers through a flexible or rigid bronchoscope. However, there is a higher potential for accidental reflected laser strikes and there is more delayed airway edema.

Rigid bronchoscopes have different sizes, commonly from 3.5- to 9-mm diameters, with a ventilating side port to facilitate ventilation when the bronchoscope is placed into the airway. If excessive leak of tidal volume occurs around the bronchoscope with positive-pressure ventilation, it may be necessary to place throat packs to facilitate ventilation. Continuous communication with the surgeon or pulmonologist is necessary in case desaturation occurs. If desaturation does occur it must be corrected by stopping surgery and allowing the anesthesiologist to ventilate and oxygenate the patient, either via the rigid bronchoscope or by removing the bronchoscope and ventilating with a mask, LMA, or ETT.

Pulse oximetry is vital during rigid bronchoscopy because there is a high risk of desaturation. There is no simple way to monitor end-tidal CO_2 or volatile anesthetics since the airway remains essentially open to atmosphere. For prolonged procedures, it is useful to perform repeated arterial blood gas analysis to confirm the adequacy of ventilation. An alternative is to interrupt surgery and ventilate the patient with a standard circuit and a mask or ETT to assess the end-tidal CO_2 .

Unlike during fiberoptic bronchoscopy via an ETT, with rigid bronchoscopy the airway is never completely secure and there is always the potential for aspiration in patients at increased risk, such as those with a full stomach, hiatus hernia, morbid obesity, and so on. It is always best to defer rigid bronchoscopy to decrease the aspiration risk if possible in these patients. When there is no benefit to be gained by

deferring and/or the airway risk is acute (e.g., aspiration of an obstructing foreign body), there is no simple solution and each case will need to be managed on an individual basis depending on the context and considering the competing risks.

Other uses of the rigid bronchoscope that require anesthesia include: dilation for benign airway stenosis, coring-out of malignant lesions in the trachea, laser ablation of endobronchial and carinal tumors, and therapeutic bronchoscopic interventions before surgical resection of lung cancer. Additionally, interventional bronchoscopy is often used for the management of airway complications following lung transplantation.

Complications of rigid bronchoscopy include: airway perforation, mucosal damage, hemorrhage, postmanipulation airway edema, and potential airway loss at the end of the procedure. In some situations, it may be necessary to keep the patient intubated with a small (i.e., 6.0-mm ID) SLT after a rigid bronchoscopy if an edematous airway is suspected or if the patient is not able to be extubated. These patients may require the use of steroids, nebulized racemic epinephrine, or helium-oxygen mixtures to treat stridor in the postoperative period.

MEDIASTINOSCOPY

Mediastinoscopy is the traditional method for the evaluation of mediastinal lymph nodes in the staging of NSCLC. It has largely been replaced for most patients by a combination of positron-emission tomography scans and endobronchial ultrasound-guided biopsies. In addition, mediastinoscopy is used to aid in the diagnosis of anterior/superior mediastinal masses.²⁰⁷ The most common mediastinal diagnostic procedure is a cervical mediastinoscopy, in which a small transverse incision (2-3 cm) is made in the midline of the lower neck in the suprasternal notch. The pretracheal fascial plane is dissected bluntly and the mediastinoscope inserted toward the carina. An alternative procedure is a parasternal (or anterior) mediastinoscopy with a small incision made through the interchondral space or the space of the excised second costal cartilage.

Morbidity related to mediastinoscopy ranges from 2% to 8%. The most severe complication of mediastinoscopy is major hemorrhage, which may require emergent thoracotomy. Other potential complications include airway obstruction, compression of the innominate artery, pneumothorax, paresis of the recurrent laryngeal, phrenic nerve injury, esophageal injury, chylothorax, and air embolism.²⁰⁸

Anesthetic Management

For patients undergoing cervical mediastinoscopy, it is important to review the chest radiograph and CT scan for the presence of a mass that might obstruct the airway during the preoperative evaluation. It is possible to perform mediastinoscopy (particularly anterior mediastinoscopy) with local anesthesia. This may be an option with an anterior mediastinal mass in a cooperative adult with a compromised airway. However, patient coughing or movement could result in surgical complications. The majority of these patients require general anesthesia with placement of an SLT. An arterial line is not necessarily used in these cases. However, it is mandatory to monitor the pulse in the

BOX 53.13 Anesthetic Management of Mediastinoscopy Hemorrhage

1. Stop surgery and pack the wound. There is a serious risk that the patient will approach the point of hemodynamic collapse if the surgery-anesthesia team does not realize soon enough that there is a problem.
2. Begin the resuscitation and call for help, both anesthetic and surgical.
3. Obtain large-bore vascular access in the lower limbs.
4. Place an arterial line (if not placed at induction).
5. Prepare for massive hemorrhage with blood warmers and rapid infusers.
6. Obtain cross-matched blood in the operating room.
7. Place a double-lumen tube or bronchial blocker if the surgeon believes that thoracotomy is a possibility.
8. Once the patient is stabilized and all preparations are made, the surgeon can reexplore the cervical incision.
9. Convert to sternotomy or thoracotomy if indicated.

right arm (pulse oximeter on the right hand, arterial line, or anesthesiologist's finger) because compression of the innominate artery by the mediastinoscope may occur and the surgeon usually is not aware that this is happening. The innominate artery supplies not only the right arm but also the right common carotid. Patients who do not have good cerebral collateral circulation (it is generally not possible to predict who these patients are) are at risk for cerebrovascular ischemia with innominate compression. A noninvasive blood pressure cuff is placed on the left arm to confirm the correct systolic pressure in case of suspected innominate compression.

Minor mediastinal hemorrhage may respond to conservative measures, such as placing the patient in the head-up position, keeping the systolic pressure in the 90s, and tamponading the wound with surgical sponges. However, massive hemorrhage requires an emergent sternotomy or thoracotomy to stop the bleeding (Box 53.13). A bronchial blocker can be passed through the lumen of the existing lung isolation device if lung isolation is required since it is often difficult to change to a DLT while the surgeon is tamponading the wound. An arterial line should be placed (if not placed previously) to measure arterial blood pressure. If hemorrhage originates from a tear in the superior vena cava, volume replacement and drug treatment may be lost into the surgical field unless they are administered through a peripheral intravenous line placed in the lower extremity.

Pneumothorax is an infrequent complication of mediastinoscopy. Pneumothorax that occurs intraoperatively (as evidenced by increased peak inspiratory pressure, tracheal shift, distant breath sounds, hypotension, and cyanosis) requires immediate treatment by chest tube decompression. All patients must have a chest radiograph taken in the postanesthesia care unit after mediastinoscopy to rule out pneumothorax.

When mediastinoscopy causes injury to the recurrent laryngeal nerve, it can be permanent in approximately 50% of the cases. If injury to the recurrent laryngeal nerve is suspected, the vocal cords should be visualized while the patient is spontaneously breathing. If the vocal cords do not move or are in a midline position, consideration has to be given to the problem of postoperative laryngeal obstruction.

TABLE 53.10 Comparison of Surgical Approaches for Pulmonary Resections

Incision	Pro	Con
Posterolateral thoracotomy	Excellent exposure to entire operative hemithorax	Postoperative pain with or without respiratory dysfunction (short and long term)
Lateral muscle-sparing thoracotomy	Decreased postoperative pain	Increased incidence wound seromas
Anterolateral thoracotomy	Better access for laparotomy, resuscitation, or contralateral thoracotomy, especially in trauma	Limited access to posterior thorax
Axillary thoracotomy	Decreased pain. Adequate access for first rib resection, sympathectomy, apical blebs, or bullae.	Limited exposure
Sternotomy	Decreased pain Bilateral access	Decreased exposure of left lower lobe and posterior thoracic structures
Transsternal bilateral thoracotomy ("clamshell")	Good exposure for bilateral lung transplantation	Postoperative pain and chest wall dysfunction
Video-assisted thoracoscopic surgery (VATS) or robotic surgery	Less postoperative pain and respiratory dysfunction	Technically difficult with central tumors and chest wall adhesions

During mediastinoscopy, the tip of the mediastinoscope is located intrathoracically and therefore it is directly exposed to pleural pressure. A venous air embolus can occur if venous bleeding occurs and patients are breathing spontaneously because of the development of negative intrathoracic pressure during inspiration. Autonomic reflexes may result from compression or stretching of the trachea, vagus nerve, or great vessels. With an uncomplicated mediastinoscopy, the patient can be extubated in the operating room and discharged home the same day.

ENDOBRONCHIAL ULTRASOUND-GUIDED BIOPSY

Various alternative techniques are available for obtaining pathology specimens from the mediastinal lymph nodes. These include CT-guided percutaneous needle aspiration, conventional bronchoscopy with transbronchial needle aspiration, and endobronchial ultrasound-guided biopsy. Endobronchial ultrasonography (EBUS) employing a radial probe through a working channel of the flexible fiberoptic bronchoscope can be used to identify mediastinal and hilar lymph nodes.²⁰⁹ Under direct EBUS guidance with fine-needle aspiration for mediastinal staging, an ultrasound puncture bronchoscope can be used to assist with the safe and accurate diagnostic interventional bronchoscopy of the mediastinal and hilar lymph nodes. Management of these patients is often done at a satellite location, either in the bronchoscopy facility or CT suite. In general, these patients are managed with topical anesthesia (aerosolized lidocaine) and conscious sedation (e.g., fentanyl and/or midazolam). When general anesthesia is used, it is preferable to place an LMA or a large diameter (≥ 8.5 mm ID) ETT because of the large diameter of the EBUS bronchoscope.

Pulmonary Surgery

Any given pulmonary resection can be accomplished by a variety of different surgical approaches. The approach

used in an individual case will depend on the interaction of several factors that include the site and pathology of the lesion(s) and the training and experience of the surgical team. Common thoracic surgical approaches and their generally accepted advantages and disadvantages are listed in Table 53.10.

MINIMALLY INVASIVE THORACOSCOPIC SURGERY

VATS is the procedure of choice for the diagnosis and management of diseases of the pleura, nondiagnosed peripheral pulmonary nodules, and interstitial lung disease (Fig. 53.45). Since the start of the modern era of thoracoscopic surgery in the early 1990s, VATS has been proposed as a less invasive approach than open thoracotomy. Today it is a well-accepted and established operation and has become the first-choice technique for lung biopsies, pleurectomies, sympathectomies, and other various pulmonary procedures.²¹⁰

In addition, VATS may be used in a variety of other surgical procedures. Some centers routinely perform the majority of lobectomies under VATS. The outcomes for VATS lobectomies in patients with limited respiratory reserves seems superior to that for open thoracotomy.²¹¹ Other surgeries, such as spinal fusion and scoliosis, have been performed with VATS. The advantages of VATS, when compared to open thoracotomy, include: (1) reduced hospital length of stay, (2) less blood loss if no mishaps occur, (3) less pain, (4) improvement in pulmonary function when compared with open thoracotomy,²¹² (5) early patient mobilization with early recovery and rapid return to work and daily activities, and (6) less inflammatory reaction, as measured by cytokine response in patients undergoing VATS lobectomy compared to open thoracotomy.²¹³

VATS lobectomy has been demonstrated to be a safe and effective procedure to treat early-stage NSCLC.²¹⁴ Thoracoscopic lobectomy is performed with a limited number of ports and an access incision of approximately 5 cm in length.²¹⁵ The advantage of the VATS technique is that



Fig. 53.45 Intraoperative photograph during video-assisted thoracoscopic surgery seen from the foot of the operating table. Multiple high-definition video screens facilitate communication between the anesthesiologist and the surgeon on the progress of the procedure.



Fig. 53.46 Robotic surgery. The operating surgeon is on the far left in the photograph seated at the robot console. Note the limited access to the patient for the anesthesiologist after the robot has been docked.

the ribs are not spread. VATS procedures are commonly performed in the lateral decubitus position; however bilateral VATS procedures, such as bilateral wedge resections or lung volume reduction, can be performed in the supine position. There is a trend to use only one port for VATS surgery.²¹⁶ Uniportal VATS may be associated with decreased postoperative pain and a shorter length of hospital stay.

Robotic thoracic surgery has been suggested as the logical advancement of VATS because of the perceived superior three-dimensional vision and increased range of motion in the chest for the surgeon with robotic techniques (Fig. 53.46).²¹⁷ Important points in anesthetic management are outlined in Box 53.14.

ANESTHETIC TECHNIQUE

Thoracoscopic surgery can be performed under local, regional, or general anesthesia with OLV or TLV.²¹⁸ For minor diagnostic procedures, VATS can be done in the awake patient. Intercostal nerve blocks performed at the

BOX 53.14 Anesthetic Considerations for Robotic Thoracic Surgery

1. A protocol for rapid emergency undocking (<60 s) of the robot must be developed and practiced in advance.
2. Limited access to the patient. The position of lung isolation device needs to be confirmed prior to docking the robot.
3. Extensions to monitoring lines and anesthesia circuit may be required.
4. There is an increased need for intrathoracic CO₂ insufflation with possible venous return and hemodynamic compromise.
5. Take precautions so that the operating room table cannot be moved while the robot is docked.
6. There is an increased risk of positional neuropathies because of potentially prolonged procedures; therefore fluid restriction is advisable.

level of the incision and two interspaces above and below provide adequate analgesia. Partial collapse of the lung on the side of surgery occurs when air enters the pleural cavity. When using local anesthesia with the patient awake, it is hazardous to insufflate gases under pressure into the hemithorax in an attempt to increase visualization of the pleural space. Although many patients suffer from advanced pulmonary disease, changes in PaO₂, PaCO₂, and cardiac rhythm are usually minimal during the procedure when it is performed under local anesthesia and the patient is breathing spontaneously.²¹⁹ However, it is recommended that a high FiO₂ is delivered via a facemask to overcome the shunt because of the loss in lung volume caused by the unavoidable pneumothorax.

For most invasive procedures VATS is performed under general anesthesia with a DLT or a bronchial blocker to achieve OLV. If the procedure is short in duration and the lung needs to be deflated for only a brief period, blood gases are not routinely monitored during the procedure. However, for patients undergoing prolonged VATS procedures such as lobectomy or for patients with marginal pulmonary status, an arterial line and measurement of arterial blood gases is required. Paravertebral blocks have been used with a single dose of local anesthetics and have been shown to reduce pain for 6 hours after thoracoscopic surgery.²²⁰

Anesthetic complications are rare during this procedure, although it is possible that any structure that the surgeon has to manipulate may be damaged. The anesthesiologist needs to be aware of the potential for conversion to open thoracotomy if massive bleeding ensues, or the surgeon is unable to localize the lung nodule to be biopsied. The majority of thoracoscopic surgery requires placement of a chest tube postoperatively. It is important to have a functional chest tube with underwater seal drainage so that extubation can be performed safely.

Lobectomy

Lobectomy is the standard operation for the management of lung cancer because local recurrence of the tumor is reduced compared to lesser resections. Lobectomy is commonly performed via open thoracotomy or VATS. Occasionally, if the clinical staging of the lung cancer is advanced,

an elective lobectomy is converted to a bi-lobectomy (right lung) or pneumonectomy during the operation. Although a posterolateral thoracotomy is the classic incision for lobectomies, anterolateral and muscle-sparing lateral incisions have also been used.

Postoperative analgesia is commonly performed with TEA or paravertebral analgesia for open procedures (see "Postoperative Analgesia" later in the chapter). An arterial line for management of arterial blood gases and measurement of systemic blood pressure is used in all patients requiring an open thoracotomy or major VATS surgery. It is useful to have two lines of intravenous access, at least one of which is large-bore, to facilitate rapid transfusion if necessary. Patients undergoing a lobectomy must be kept normothermic, normotensive, and with an acceptable PaO_2 and oxygen saturation, particularly during OLV. Patients should have a thermal blanket on the lower extremities to prevent hypothermia and its deleterious effects during HPV. After the lobe and blood vessels have been dissected, a test maneuver is performed with the surgeon clamping the surgical bronchus to confirm that the specific lobe is extirpated. This maneuver is accomplished by unclamping the limb of the DLT connector of the respective side, or in the case of a bronchial blocker, by deflating the blocker balloon, and reexpanding the lung with manual ventilation. During VATS lobectomy, as a result of the interference to the surgical field caused by reinflating the residual lobe, the anesthesiologist may be asked to fiberoptically inspect the bronchial tree to confirm patency of the bronchus of the noninvolved lobe(s). Once the lobectomy has been performed, the bronchial stump is usually tested with 20 cm H_2O positive pressure in the anesthetic circuit to detect the presence of air leaks. A patient undergoing an uncomplicated lobectomy can be usually extubated in the operating room provided preoperative respiratory function is adequate (see "Preoperative Evaluation of the Thoracic Surgery Patient" earlier in the chapter) and the patient is AWaC.

Pancoast tumors are carcinomas of the superior sulcus of the lung and can invade and compress local structures including the lower brachial plexus, subclavian blood vessels, stellate ganglion (causing Horner syndrome), and vertebrae. Lobectomy may require 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 in the contralateral arm due to frequent compression of the ipsilateral vessels during surgery.

SLEEVE LOBECTOMY

Bronchial sleeve resections are performed for neoplasms or benign strictures. Bronchogenic carcinoma is the most frequent indication for a sleeve lobectomy, followed by carcinoid tumors, endobronchial metastases, primary airway tumors, and bronchial adenomas. Sleeve lobectomy involving parenchyma-sparing techniques in patients with limited pulmonary reserve is an alternative procedure 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. 53.47).

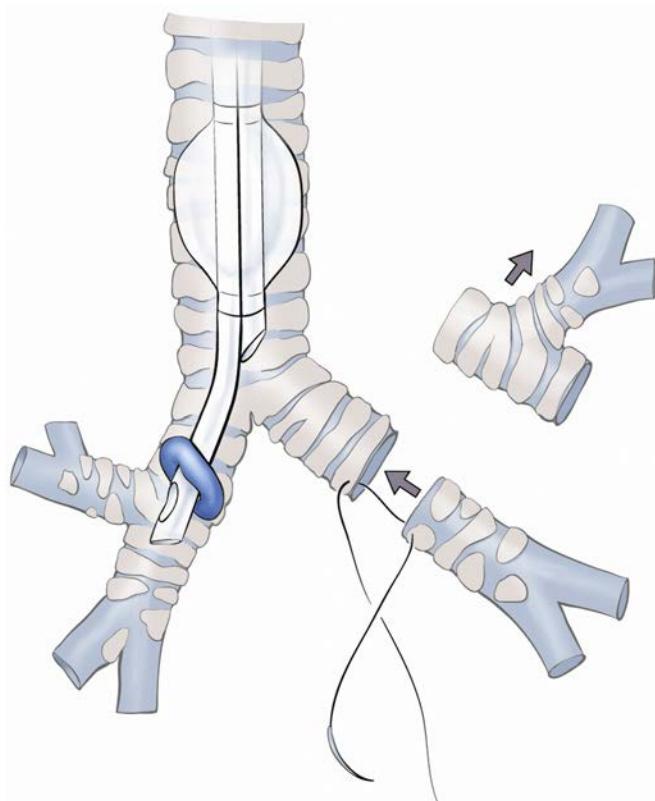


Fig. 53.47 Diagram of the surgical procedure for a left upper sleeve lobectomy. Airway management is with a right-sided double-lumen tube. Note that it will not be possible to position an endobronchial tube or bronchial blocker in the ipsilateral mainstem bronchus during this procedure.

Patients undergoing sleeve lobectomy require lung isolation with a contralateral DLT or endobronchial tube (i.e., use a right-sided DLT for a left sleeve lobectomy). High-frequency jet ventilation (HFJV) can be used for resections close to the tracheal carina. For a sleeve lobectomy involving resection of vessels, heparinization is necessary. In these cases, thoracic epidural catheters should not be manipulated for 24 hours 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. Immediate and long-term survival is better after sleeve lobectomy compared with right pneumonectomy for comparable stages of right upper lobe cancer.²²¹

Pneumonectomy

Complete removal of the lung is required when a lobectomy or its modifications is not adequate to remove the local disease and/or ipsilateral lymph node metastases. Atelectasis and pneumonia occur following pneumonectomy as they do following lobectomy but may in fact be less of a problem because of the absence of residual parenchymal dysfunction on the operative side. However, the mortality rate following pneumonectomy exceeds that for lobectomy because of postoperative cardiac complications and acute lung injury.

The overall operative mortality for the first 30 days after pneumonectomy ranges from 5% to 13% and correlates inversely with the surgical case volume.²²² The risk of complications increases fivefold in patients age 65 and older.²²³

Thoracotomy for pneumonectomy is usually performed through a standard posterolateral incision. 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.

There is no consensus among thoracic surgeons on the best method of management of the postpneumonectomy space. If suction is applied to an empty hemithorax or a chest drain is connected to a standard underwater-seal system it may cause a mediastinal shift with hemodynamic collapse. Some thoracic surgeons do not place a chest drain after a pneumonectomy; some prefer to use a temporary drainage catheter to add or remove air. The removal of air, ranging from 0.75 up to 1.5 L, is necessary to empty the chest and to keep the mediastinum ("balanced") and the trachea in the midline. Some surgeons place a specifically designed postpneumonectomy chest drainage system with both high- and low-pressure underwater relief valves to balance the mediastinum.²²⁴ A chest radiograph is mandatory after the patient arrives in the postanesthesia care unit or in the surgical intensive care unit to assess the mediastinal shift.

The patient scheduled to undergo a pneumonectomy is considered at high risk for perioperative morbidity and mortality. 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 CVP catheter is recommended to help guide intravascular fluid management and to administer vasopressors if needed, specifically in the postoperative period.

A major lung resection, such as pneumonectomy, decreases ventilatory function and has significant effects on the right ventricular function.²²⁵ Immediately after pneumonectomy, the right ventricle may dilate and the right ventricular function decrease. Increased right ventricular afterload is due to an increase in pulmonary artery pressure and PVR. This is considered to be one of the main causes of right ventricular dysfunction after a major lung resection.

Management of lung isolation in a pneumonectomy patient can be achieved with a DLT, bronchial blocker, or SLT. When using a DLT for a pneumonectomy patient, it is optimal to use a device that does not interfere with the ipsilateral airway (i.e., for a right pneumonectomy a left-sided DLT). If a left-sided DLT or bronchial blocker is used for a left pneumonectomy, it must be withdrawn prior to stapling the bronchus, in order to avoid accidental inclusion into the suture line.

Specific areas of concern in the management of the patient undergoing pneumonectomy include: (1) fluid management, (2) intraoperative tidal volume, and (3) acute lung injury postsurgery. Fluid administration after major lung resection continues to be an issue. In a retrospective report by Zeldin and associates,²²⁶ the risk factors that were identified for the development of acute lung

injury ("postpneumonectomy pulmonary edema") were a right-sided pneumonectomy, increased perioperative intravenous fluid administration, and increased urine output in the postoperative period. A more recent study by Licker and colleagues has shown that the excessive administration of intravenous fluids in thoracic surgical patients (more than 3 L in the first 24 hours) is an independent risk related to an acute lung injury.²²⁷ There is reasonable clinical evidence that excessive fluid administration is associated with the development of an acute lung injury, which has a high mortality rate following pneumonectomy. Consequently, pneumonectomy patients should have restricted intraoperative fluid administration while preserving renal function. Some cases may require the use of inotropes/vasopressors to maintain hemodynamic stability while restricting fluids (see **Box 53.11**).

Respiratory failure is a leading cause of postoperative morbidity and mortality in patients undergoing pneumonectomy. A retrospective report²²⁸ 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 and associates²²⁹ 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. 6 mL/kg, ideal body weight) in the pneumonectomy patient, and limit peak and plateau inspiratory pressures (i.e., <35 and 25 cm H₂O, respectively) during OLV.

The incidence of acute lung injury (postpneumonectomy pulmonary edema) after pneumonectomy is only 4%. However, the mortality rate is 30% to 50%. The etiology seems multifactorial. One study²²⁹ has identified four independent risk factors for acute lung injury after pulmonary resection: (1) pneumonectomy, (2) excessive administration of fluids in the intraoperative period, (3) high intraoperative ventilatory pressure index (combined airway pressure and time), and (4) preoperative alcohol abuse. The incidence of an acute lung injury is greater for a right-sided versus left-sided pneumonectomy. This may be related to the higher postoperative pulmonary artery pressures after a right versus left pneumonectomy (Fig. 53.48).²³⁰ At the present time only symptomatic management is appropriate for this lung injury. This includes fluid restrictions, diuretic administration, low ventilatory pressures and tidal volumes (if mechanical ventilation is used), and measures to decrease the pulmonary artery pressure. ECMO may be useful in managing this complication.²³¹

EXTRAPLEURAL PNEUMONECTOMY

Extrapleural pneumonectomy is a therapeutic option for selected patients with MPM.²³² Significant improvement in survival has been achieved in patients who have an advanced MPM with extrapleural pneumonectomy and high-dose radiotherapy in the postoperative period. Extrapleural pneumonectomy involves an extensive resection that may include lymph nodes, pericardium, diaphragm, parietal pleura, and the chest wall. The anesthetic management of the extrapleural pneumonectomy patient is

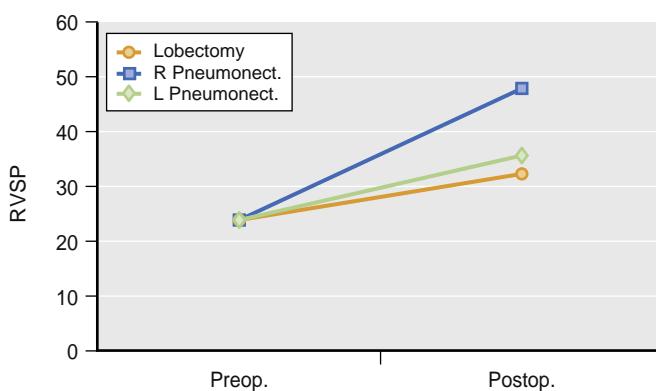


Fig. 53.48 Comparison of right ventricular systolic pressure (RVSP) measured by echocardiography in patients before (Preop.) and at 6 months after (Postop.) pulmonary resections. *L Pneumonect.*, Left pneumonectomy; *R Pneumonect.*, right pneumonectomy. Note the elevated RVSP, and therefore pulmonary artery pressure, after a right pneumonectomy. (Based on data from Foroulis C, et al. *Eur J Cardiothorac Surg*. 2004;26:508.)

characterized by significant loss of blood because of chest wall vessel involvement. In these patients, it is recommended that a CVP catheter be used to guide intravascular fluid administration and insure large-bore intravenous access. During tumor dissection, venous return to the heart may be compromised due to multiple factors including blood loss, compression effect by the tumor in superior vena cava, or surgical causes. If excessive bleeding ensues, it must be replaced to maintain an acceptable hematocrit and to keep the coagulation profile within normal limits. Because of extensive tumor resection and the potential for a pericardial resection in right-sided surgery, cardiac herniation or hemodynamic instability can appear postoperatively after the patient is turned from lateral decubitus to supine position. It is common to ventilate these patients for a short period postoperatively because of the extended duration of the surgery and the large fluid shifts. If a DLT is used intraoperatively, the DLT is usually replaced at the end of the case with an SLT.

SLEEVE PNEUMONECTOMY

Tumors involving the most proximal portions of the main-stem bronchus and the carina may require a sleeve pneumonectomy. These are most commonly performed for right-sided tumors and can usually be performed without ECMO via a right thoracotomy. A long SLT can be advanced across into the left mainstem bronchus during the period of tracheobronchial anastomosis. High-frequency positive-pressure ventilation (HFPPV) has also been used for this procedure and the combined use of HFPPV and a DLT has been described.²³³ Since the carina is surgically more accessible from the right side, left sleeve pneumonectomies are commonly performed as a two-stage operation: first there is a left thoracotomy and pneumonectomy followed by a right thoracotomy for the carinal excision. The complication rate and mortality are higher, and the 5-year survival (20%) significantly lower than for other pulmonary resections. Postpneumonectomy pulmonary edema is particularly a problem following right sleeve pneumonectomy.

Limited Pulmonary Resections: Segmentectomy and Wedge Resection

A limited pulmonary resection is one in which less than a complete lobe is removed. The two procedures fitting this definition are segmentectomy and wedge resection. Segmentectomy is an anatomic pulmonary resection of the pulmonary artery, vein, bronchus, and parenchyma of a particular segment of the lung. Segmentectomy is usually performed as surgical therapy for patients with primary lung cancer and limited cardiorespiratory reserves. In contrast, a wedge resection is a nonanatomic removal of a portion of the lung parenchyma with a 1.5- to 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. Lung cancers that are considered for limited resection are usually less than 3 cm in size and are located in the periphery of the lung with regional lymph nodes free of metastatic cancer. Small peripheral lung lesions may be localized preoperatively for VATS resection by CT placement of a marker such as a coil.²³⁴ The relevance of this for anesthesia is that the CT procedure may cause a pneumothorax and possibly a bronchopleural fistula. To avoid a possible tension pneumothorax at induction, positive-pressure TLV should be avoided (or minimized) and lung isolation with OLV commenced as soon as possible.

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). Cersolio and associates²³⁵ 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 contralateral 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.²³⁶ It is very important to use low tidal volumes (i.e., 3-4 mL/kg) during selective lobar ventilation, particularly in patients with previous pneumonectomy to prevent overinflation 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, including 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 underwater-seal chest drainage is used in the postoperative period.

Anesthetic Management for Specific Surgical Procedures

ESOPHAGEAL SURGERY

Esophageal surgery is performed for both malignant and benign disease and may be curative or palliative. General considerations that apply to many esophageal surgery patients include an increased risk of aspiration caused by esophageal dysfunction and the possibility of preoperative malnutrition.

Esophagectomy

Esophagectomy is a palliative and potentially curative treatment for esophageal cancer and may occasionally be required for some benign obstructive lesions which do not respond to conservative therapy. It is a major surgical procedure and is associated with high morbidity and mortality rates (10%–15%). There is an inverse correlation between perioperative mortality and surgical volume and the cure rate of esophageal cancer with esophagectomy is between 10% and 50%. There are multiple surgical procedures for esophageal cancer (Table 53.11) that combine some or all of three fundamental approaches: (1) transthoracic approach, (2) transhiatal approach, and (3) minimally invasive surgery (laparoscopic/thoracoscopic or robotic esophagectomy).²³⁷ The incidence of respiratory complications has been reported to be between 18% and 26% for both the transthoracic and transhiatal esophagectomy approaches.²³⁸ One study showed that the development of acute respiratory distress syndrome occurred in 14.5% of patients and acute lung injury in 24%.²³⁹ Complications associated with the gastroesophageal anastomosis are

anastomotic leakage/dehiscence (5%–26%) and stenosis (12%–40%). Outcomes are improved with a multimodal anesthetic management protocol using fluid restriction, early extubation, thoracic epidural analgesia, and vasoressor/inotrope infusions to support blood pressure.²⁴⁰ Hypotension decreases the blood flow to the esophago-gastric anastomosis. The use of vasopressors or inotropes, in normovolemic patients, restores the systemic pressure and the anastomotic blood flow.²⁴¹ Fluid management for esophageal surgery is essentially the same as for pulmonary resection surgery.

Transthoracic Approach. Transthoracic esophagectomy is commonly a two-phase procedure. The first phase involves a laparotomy performed with the patient in the supine position and the creation of a neoesophagus tube using the stomach. The second phase involves a right-sided thoracotomy in the left lateral position and esophageal reconstruction through the thoracic route. Some surgeons may perform this procedure through an extended left thoracoabdominal incision.

The anesthetic management for these patients includes the use of standard monitors, an invasive arterial line, and a CVP catheter to the large fluid shifts. Access to the right internal jugular is not a problem; however there is always a possibility of a surgical esophageal anastomosis in the left neck contraindicating access to the left internal jugular. A thoracic epidural catheter is usually placed to provide postoperative analgesia. Because of the wide number of dermatomes that must be covered for both incisions by the epidural infusion, it is best to use hydrophilic opioids (such as hydromorphone) in combination with local anesthetics in preference to lipophilic opioids. Most patients with an esophageal carcinoma have gastric reflux; for this reason, precautions (including a rapid-sequence induction with cricothyroid pressure) should be taken to protect the airway against aspiration.

During the second phase (right thoracotomy), a left-sided DLT or a right-sided bronchial blocker is required to facilitate lung collapse. Because esophagectomy requires a prolonged period of OLV, this procedure is marked by

TABLE 53.11 Surgical Approaches for Esophagectomy and Esophagogastrectomy

Surgery	Incisions	Anesthetic Considerations
Laparotomy and right thoracotomy ("Ivor Lewis")	Two incisions: upper abdominal midline, right thoracotomy at approx. 5th or 6th intercostal space	One-lung ventilation necessary. Repositioning of patient intraoperatively from supine to right lateral
Transhiatal ("Orringer") (lower-third lesions; may be used for mid-third in some centers)	Two incisions: upper abdominal midline and left neck	Hemodynamic instability from cardiac compression during blunt intrathoracic dissection. Possibility of occult perforation of tracheobronchial tree during blunt dissection (may need to advance endotracheal tube into bronchus) No vascular access in left neck
Left thoracoabdominal (lower esophageal lesions only)	One incision: left lateral thoracotomy extended to left upper lateral abdominal	One-lung ventilation desirable
Combined chest, abdominal, and neck ("three hole"; upper and mid-esophageal lesions)	Three incisions: right thoracotomy, laparotomy, left neck	One-lung ventilation necessary Repositioning lateral to supine intraoperatively No vascular access in left neck
Minimally invasive, laparoscopy plus VATS or robotic surgery	One to three small incisions plus video port access. Possible left neck incision at end.	One-lung ventilation necessary Potentially prolonged surgery

VATS, Video-assisted thoracoscopic surgery.

an important inflammatory response. Michelet and colleagues²⁴² have shown that the use of protective ventilatory strategies during OLV decrease the proinflammatory systemic response. This decreased response can be achieved by delivering 5 mL/kg of tidal volume and a PEEP of 5 cm H₂O to the dependent lung, instead of the 9 mL/kg of tidal volume that is conventionally used during esophagectomy.

Manipulation of the esophagus during thoracotomy may compromise venous return, which can cause hypotensive episodes. Early extubation in the operating room is encouraged if the patient meets standard criteria for extubation. If extubation is not possible, the DLT should be exchanged for an SLT and mechanical ventilation used in the postoperative period.

Transhiatal Approach. Airway management is done with an SLT. Apart from this, anesthetic management is essentially the same as for a transthoracic approach. Of special concern is that the blunt/blind manual dissection of the thoracic esophagus by the surgeon through the hiatus during this approach is often associated with cardiac compression and sudden severe hypotension. Also, this blind dissection can cause vascular or distal airway injuries if the tumor is adherent.²⁴³ It is a good practice to not cut the ETT for this procedure in case of surgical perforation of the trachea or bronchus necessitating advancement of the ETT into a mainstem bronchus for emergent OLV.

Minimally Invasive Approach. Minimally invasive esophagectomy involves the use of laparoscopic, thoracoscopic, and/or robotic surgical approaches. For a laparoscopic approach, distension of the peritoneum may produce hemodynamic changes because of the intragastric pressure generated by carbon dioxide insufflation. In these cases, it is important to adjust ventilatory parameters to achieve an optimal PaCO₂. For the thoracoscopic approach, a left-sided DLT or a bronchial blocker is required. During robotic surgery, the use of a lung isolation device is required to achieve OLV. Special considerations for robotic surgery include protecting the patient against any injury related to the robot and not moving the operating room table while the robot is being used. The thoracoscopic-assisted esophagectomy has several advantages including less blood loss, less pain, and a shorter length of hospitalization. This method may require a prolonged duration of surgery. Some centers favor performing the VATS portion of a minimally invasive esophagectomy in the prone position to improve surgical access.²⁴⁴ Lung isolation for these cases is usually with a bronchial blocker via an SLT.

Patients undergoing esophagectomy usually require a nasogastric tube, which must be well-secured at the end of the operation. Respiratory complications, including the development of an acute lung injury, may be present after an esophagectomy. Intrathoracic anastomotic leakage is a feared major complication after esophageal surgery, and carries a high mortality rate of 4% to 30%.²⁴⁵ To treat this potential complication, nasogastric decompression and nutritional support should be used. Severe leakage usually occurs in the early postoperative period as a consequence of gastric necrosis, and it may present with respiratory symptoms and signs of shock. Even though there is a very high mortality rate, prompt surgical intervention is recommended. Patients older than 80 years have an increased risk of mortality after esophagectomy, independent of comorbidity.²⁴⁶

Esophageal Surgery for Benign Disease

Hiatal Hernia. Although most patients with gastroesophageal reflux have a hiatal hernia, most patients with a hiatal hernia do not have significant reflux.²⁴⁷ Patients with heartburn have a lowered barrier pressure and may be at increased risk for regurgitation of gastric contents. Two types of hiatal hernia have been described. Type I hernias, also called sliding hernias, make up approximately 90% of esophageal hiatal hernias. In this type, the esophagogastric junction and fundus of the stomach have herniated axially through the esophageal hiatus into the thorax (Fig. 53.49). The term sliding refers to the presence of a sac of parietal peritoneum. The lower esophageal sphincter is cephalad to the diaphragm and may not respond appropriately to increased abdominal pressure. Thus a reduced barrier-pressure during coughing or breathing leads to regurgitation. The type II or paraesophageal hiatus hernia is characterized by portions of the stomach herniating into the thorax next to the esophagus. In the presence of a type II hernia, the esophagogastric junction is still located in the abdomen. The most common complications from type II hernias are blood loss, anemia, and gastric volvulus.

The goal of surgical repair of a sliding hernia is to obtain competence of the gastroesophageal junction. Since restoration of the normal anatomy is not always successful in preventing subsequent reflux, several antireflux operations have been developed, such as the Nissen fundoplication. Repair of a hiatal hernia can be performed via a thoracotomy or laparotomy, or minimally invasively.



Fig. 53.49 Chest radiograph of a patient with a hiatal hernia and a dilated intrathoracic stomach, scheduled for hiatal hernia repair via a left thoracotomy. An air-fluid level can be seen in the stomach behind the heart. These patients are at high risk for aspiration on induction of anesthesia.

Benign Esophageal Stricture. Chronic reflux of acidic gastric contents can lead to ulceration, inflammation, and eventually stricture of the esophagus. The pathologic changes are reversible if the acidic gastric contents cease their contact with the esophageal mucosa. Surgery may be necessary if medical treatment and dilatations are inadequate. There are two types of surgical repair, both of which are usually approached via a left thoracoabdominal incision. Gastroplasty after esophageal dilatation interposes the fundus of the stomach between esophageal mucosa and the acidic milieu of the stomach. The remaining fundus may be sewn to the lower esophagus to create a valvelike effect. The second type of repair is resection of the stricture and the creation of a thoracic end-to-side esophagogastrectomy. Vagotomy and antrectomy are performed to eliminate stomach acidity, and a Roux-en-Y gastric drainage procedure is performed to prevent alkaline intestinal reflux.

Esophageal Perforation and Rupture. There are multiple causes of esophageal perforation, including foreign bodies, endoscopy, bougienage, traumatic tracheal intubation, gastric tubes, and oropharyngeal suctioning. Iatrogenic causes are the most common, with upper gastrointestinal endoscopy being the most frequent cause. A rupture is a burst injury often due to uncoordinated vomiting, straining associated with weight-lifting, childbirth, defecation, and crush injuries to the chest and abdomen. The rupture is usually located within 2 cm of the gastroesophageal junction on the left side. Rupture is the result of a sudden increase in abdominal pressure with a relaxed lower esophageal sphincter and an obstructed esophageal inlet. In contrast to a perforation, in the presence of a rupture, the stomach contents enter the mediastinum under high pressure and the patient becomes symptomatic much more abruptly.

In addition to chest and/or back pain, patients with intrathoracic esophageal perforation or rupture may develop hypotension, diaphoresis, tachypnea, cyanosis, emphysema, and hydrothorax or hydropneumothorax.²⁴⁸ Radiologic studies may reveal subcutaneous emphysema, pneumomediastinum, widening of the mediastinum, pleural effusion, and pneumoperitoneum. In some cases, minor perforations can be managed conservatively. Major injuries will rapidly develop mediastinitis and sepsis if not treated surgically, so repair and drainage is an emergency procedure usually performed via a left or right thoracotomy.

Achalasia. Achalasia is a disorder in which there is a lack of peristalsis of the esophagus and a failure of the lower esophageal sphincter to relax in response to swallowing. Clinically, the patients have esophageal distention that may lead to chronic regurgitation and aspiration. The goal of treatment is to alleviate the distal obstruction. This can be done by either esophageal dilatation or by surgery. Dilatation, which carries with it the risk of perforation, can be achieved by mechanical, hydrostatic, or pneumatic means. The surgical repair consists of a Heller myotomy, which is an incision through the circular muscle of the esophagogastric junction. The myotomy is often combined with a hiatal hernia repair to prevent subsequent reflux. This can be performed via thoracotomy, laparotomy, or laparoscopy.²⁴⁹ This procedure can also be performed endoscopically. Peroral endoscopic myotomy (POEM) requires

general anesthesia with endotracheal intubation.²⁵⁰ Insufflation of CO₂ via the endoscope frequently leads to pneumoperitoneum, which requires abdominal decompression during the procedure.

Esophagorespiratory Tract Fistula. Esophagorespiratory tract fistula in an adult is most often due to malignancy. Occasionally, the fistula is benign, and may be due to injury by a tracheal tube, trauma, or inflammation. Of the malignant fistulae, approximately 85% are secondary to esophageal cancer. In contrast to the pediatric patient with esophagorespiratory tract fistulae, which usually connect the distal esophagus to the posterior tracheal wall, these fistulae may connect to any part of the respiratory tract.²⁵¹ In most cases, the fistula can be seen on esophagoscopy or bronchoscopy. In malignant cases, the goal of surgery is usually palliation. The technique of lung isolation will depend on the location of the fistula. One option in adults with a distal tracheal fistula is the use of bilateral small (5–6 mm ID) endobronchial tubes.²⁵²

Zenker Diverticulum. Zenker diverticulum is actually a diverticulum of the lower pharynx. It arises from a weakness at the junction of the thyropharyngeus and cricopharyngeus muscles just proximal to the esophagus. It is commonly considered as an esophageal lesion because of its proximity to the upper esophagus and because the underlying cause may be a failure of relaxation of the upper esophageal sphincter during swallowing. Early symptoms may be nonspecific with dysphagia and complaints of food sticking in the throat. As the diverticulum enlarges patients describe noisy swallowing, regurgitation of undigested food, and supine coughing spells. Recurrent aspiration and pneumonia may develop.

The major concern for anesthesia is the possibility of aspiration on induction of general anesthesia for excision of the diverticulum.²⁵³ Even prolonged fasting does not ensure that the diverticulum will be empty. The best method to empty the diverticulum is to have the patient express and regurgitate the contents immediately prior to induction. Many of these patients will be used to doing this on a regular basis at home. Since the diverticulum orifice is almost always above the level of the cricoid cartilage, cricoid pressure during a rapid-sequence induction does not prevent aspiration and may contribute to aspiration by causing the sac to empty into the pharynx. Surgical excision is usually done through a lower left neck incision.

The safest method of managing the airway for these patients may be awake fiberoptic intubation. However, intubation has been managed without incident using a modified rapid-sequence induction without cricoid pressure and with the patient supine and in a head-up position of 20 to 30 degrees. Other considerations in these patients include the possibility of perforation of the diverticulum when passing an orogastric or nasogastric tube or an esophageal bougie.

Anesthesia for Tracheal Resection

Tracheal resection and reconstruction is indicated in patients who have a tracheal obstruction as a result of a

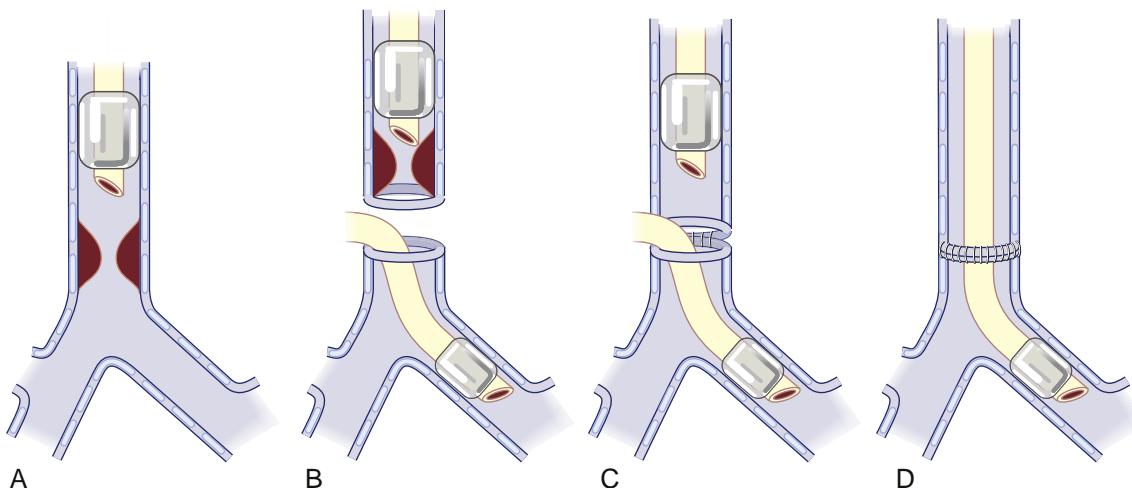


Fig. 53.50 Airway management and surgical procedure for resection of a low tracheal lesion. (A) Initial intubation above the lesion. (B) Left endobronchial intubation distal to the lesion after the trachea has been opened. (C) Placement of sutures for the posterior anastomosis. (D) The endobronchial tube has been removed, and the original endotracheal tube has been advanced distal to the anterior anastomosis into an endobronchial position. (Modified from Geffen B, Bland J, Grillo HC. Anesthetic management of tracheal resection and reconstruction. *Anesth Analg*. 1969;48:884.)

tracheal tumor, previous tracheal trauma (most commonly due to postintubation stenosis), congenital anomalies, vascular lesions, and tracheomalacia. For patients who have operable tumors, approximately 80% undergo segmental resection with primary anastomosis, 10% undergo segmental resection with prosthetic reconstruction, and the remaining 10% undergo placement of a T-tube stent.

Diagnostic studies are reviewed as part of the preoperative evaluation. The CT scan is a useful diagnostic tool to evaluate the degree, level, and length of the lesion. Bronchoscopy is one of the definitive diagnostic tests for tracheal obstruction. Bronchoscopy for a patient with tracheal stenosis should be carried out in the operating room where the surgical and anesthesia teams are present and ready to intervene should loss of airway occur. An advantage of rigid bronchoscopy over flexible bronchoscopy is that it can bypass the obstruction and provide a ventilation pathway if complete obstruction occurs. During surgery, all patients should have an invasive arterial catheter placed to facilitate measurement of arterial blood gases, as well as measure arterial blood pressure. CVP catheters are only used if the patient requires cardiopulmonary bypass (CPB).

A variety of methods for providing adequate oxygenation and elimination of CO_2 have been used during tracheal resection. The different alternatives include: (1) standard orotracheal intubation, (2) insertion of a sterile SLT into the opened trachea or bronchus distal to the area of resection, (3) HFJV through the stenotic area, (4) HFPPV, and (5) the use of ECMO.

Induction of anesthesia in patients with a compromised airway requires good communication between the surgical team and the anesthesiologist. The surgeon should always be in the operating room during induction and available to manage a surgical airway if this becomes necessary.²⁵⁴ A rigid bronchoscope must be immediately available. The patient should be thoroughly preoxygenated with 100% oxygen before induction. The airways of patients with congenital or acquired tracheal stenosis are unlikely to collapse during induction of anesthesia. However, intratracheal masses may lead to airway obstruction with induction of

anesthesia and should be managed similarly to anterior mediastinal masses (discussed later in chapter). One airway management technique is to begin the case with rigid bronchoscopy and tracheal dilation and then to pass an SLT through the stenosis. This tube is withdrawn into the proximal trachea once the distal trachea is opened and a second sterile SLT is placed into the distal trachea by the surgeon. Ventilation is done via a sterile anesthetic circuit with an airway gas sampling catheter passed across the drapes into the surgical field (this technique is commonly referred to as a “cross-field ventilation”). With a low tracheal lesion, a right thoracotomy provides the optimal surgical exposure. A sterile SLT is used to provide ventilation to the lung distal to the resection. After the posterior anastomosis is completed, the endobronchial tube is removed and the original SLT is advanced past the site of resection (Fig. 53.50). This technique can also be used for carinal resection.

A third technique for airway management during tracheal resection includes HFJV through a small-bore ETT or catheter.²⁵⁵ With this technique, a small-bore uncuffed catheter is placed through the stenotic area, and ventilation is accomplished by intermittently exposing the lung to a high flow of fresh gas through the catheter. Other techniques that have been used for oxygenation during distal airway resections include HFPPV, helium-oxygen mixtures, and CPB.

After the tracheal resection is completed, most patients are kept in a position of neck flexion to reduce tension on the suture line. Replacement of the SLT by an LMA for emergence facilitates bronchoscopy if required. A thick chin-sternum suture may be placed for several days to maintain neck flexion or a cervical splint may be used.²⁵⁶ A Montgomery T-tube with the upper limb 0.5 to 1 cm above the vocal cords may be inserted at the end of surgery as a tracheal stent in cases when glottic edema is a concern, or for patients requiring ventilatory support. If a tracheostomy is performed, it will be done distal to the anastomosis. Early extubation is highly desirable. If a patient requires reintubation, it should be performed with a flexible fiberoptic bronchoscope by advancing an SLT under direct vision over



Fig. 53.51 Computed tomographic scan of a patient with a lung abscess distal to an obstructing carcinoma of the right upper lobe. The diagnostic thick wall of the abscess and the air-fluid level can be appreciated in the right upper thorax. These patients are at risk for soiling of uncontaminated lung regions during repositioning for surgery from pus in the abscess. The optimal method of lung isolation is with a double-lumen endobronchial tube.

the bronchoscope and then placing it in the patient's trachea. The patient is kept in a head-up position to diminish swelling. Steroids may be useful in these cases to decrease airway edema.

One of the complications in the postoperative period is tetraplegia, with hyperflexion of the neck having been implicated as a potential cause. In these cases, it is necessary to cut the chin stitch. Infusions of propofol/remifentanil or dexmedetomidine, with fiberoptic bronchoscopy guidance and full patient cooperation, can aid extubation.²⁵⁷

BRONCHIECTASIS/LUNG ABSCESS/EMPYEMA

Bronchiectasis is a disease that causes localized, irreversible dilatation of part of the bronchial tree. Involved bronchi are 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 may require surgery if it causes hemoptysis or recurrent pneumonia. An abscess is a nonanatomic area of **liquefactive necrosis** of the lung often distal to an obstruction or following a pneumonia (Fig. 53.51). 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% to 16% of cases and with a 40% increase in the associated perioperative mortality rate. Mortality further increases when the empyema is associated with a bronchopleural fistula. Surgical interventions for patients with empyema include decortication (the method of choice when the underlying lung is unable to expand because of 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).²⁵⁸ In less severe cases, tube drainage, antibiotic irrigation, and debridement may be sufficient.

All of these infective indications for thoracic surgery are less common in the developed world since the introduction of antibiotics. Anesthetic considerations during surgery for these infective indications include the need for lung isolation to protect uninvolved lung regions from soiling by pus in the infected areas. The risk of soiling occurs if the patient is repositioned for surgery, after induction of anesthesia, before the lung is adequately isolated. Because of the inflammation, surgery is technically more difficult and there is a greater risk of massive hemorrhage.

Anesthetic Management

Some of these patients may present with sepsis at the time of surgery. In septic patients, the placement of a thoracic epidural catheter is not recommended. These patients require lung isolation, preferably with a DLT. The DLT facilitates suctioning of debris and copious secretions that are present in the tracheobronchial tree. 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 reexpansion. Extubation in the operating room is encouraged if the patient meets standard criteria for extubation.

BRONCHOPLEURAL FISTULA

A bronchopleural fistula 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; or (3) stump dehiscence of a bronchial suture line after pulmonary resection. Pneumonectomy patients have an incidence of bronchopleural fistula ranging from 2% to 11%,²⁵⁹ with mortality ranging from 5% to 70%.

The diagnosis of bronchopleural fistula is usually made clinically. After pneumonectomy, the diagnosis is based on the sudden onset of dyspnea, subcutaneous emphysema, contralateral deviation of the trachea, and a decrease of fluid level on serial radiographs of the chest (Fig. 53.52). In lobectomy patients, persistent air leak, purulent drainage, and expectoration of purulent material are usually diagnostic indicators of a bronchopleural fistula. When the fistula appears after removal of a chest tube, the diagnosis of bronchopleural fistula is made on the basis of fever, purulent sputum, and a new air-fluid level in the pleural cavity on the chest radiograph.

The diagnosis is 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 of the indicator 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 bronchopleural fistula can also be used as indicators.²⁶⁰

If the disruption occurs early in postpneumonectomy patients, it can be life threatening and it is possible to resuture the stump. Late or chronic postpneumonectomy bronchial disruption is managed with drainage or with the Clagett procedure, which includes open pleural drainage and the use of a muscle flap to reinforce the bronchial stump. In nonpneumonectomy cases, if the lung expands to