



Fig 53.52 (A) Chest radiograph of a patient immediately postoperatively after a right pneumonectomy. (B) The same patient on postoperative day 6. This is a normal postpneumonectomy film. The right hemithorax is gradually filling with serous fluid. (C) The same patient on postoperative day 7. The patient had the sudden onset of severe dyspnea, desaturation, and coughing. The chest radiograph reveals a decrease in the fluid level in the right hemithorax. This is diagnostic of a bronchopleural fistula caused by the dehiscence of the bronchial stump.

fill the thoracic cavity, the air leak can usually be controlled with chest tube drainage alone. However, if the fistula is large and a significant leak through a large persistent pleural space occurs, it is unlikely that the fistula will close, and surgical resection is necessary.

Anesthetic Management

The patient with a bronchopleural fistula presents several intraoperative challenges for the anesthesiologist. These include: (1) the need for lung isolation to protect healthy lung regions, (2) the possibility of tension pneumothorax with positive-pressure ventilation, and (3) the possibility of inadequate ventilation due to air leak from the fistula. Preoperatively, it is useful to estimate the loss of tidal volume through the bronchopleural fistula, which may be done in two ways. First, one should determine whether air bubbles flow intermittently or continuously through the chest tube. If air bubbles flow intermittently, then the fistula is small. In contrast, when a patient has a large bronchopleural fistula or bronchial rupture, air will bubble continuously through the water-seal chamber of the chest-tube drainage system. Second, the size of the bronchopleural fistula may be quantified by the difference between inhaled and exhaled tidal volumes. In a nonintubated patient, this may be determined with a tight-fitting mask and a fast-responding spirometer. In an intubated patient, it is determined by direct attachment of the spirometer to the ETT. The larger the air leak, the greater the need to isolate the bronchopleural fistula with the use of a lung isolation device (a DLT or an independent bronchial blocker).

Several nonsurgical approaches (i.e., the use of various mechanical ventilation–chest tube drainage systems) have been used for the treatment of patients with a bronchopleural fistula. These approaches consist of OLV and differential lung ventilation, including HFV, PEEP to the pleural cavity equal to intrathoracic PEEP, and unidirectional chest tube valves. One-way endobronchial valves have been used successfully in patients with bronchopleural fistula who were considered unfit for surgery.²⁶¹

For patients undergoing operative repair, the ability to adequately deliver positive-pressure ventilation intraoperatively must be carefully considered prior to surgery. A chest drain should be placed prior to induction to avoid the possibility of tension pneumothorax with positive-pressure ventilation. A DLT is the best choice for delivering positive-pressure ventilation. The DLT can provide positive-pressure

ventilation to the normal lung without loss of minute ventilation through the fistula and prevent the hazard of contamination of the uninfected lung with infected material when the patient is turned to the lateral decubitus position.

The safest method of obtaining lung isolation may be awake fiberoptic intubation with a DLT.²⁶² However, this requires a cooperative patient and excellent topical anesthesia and is often not an option. Another option is to maintain spontaneous ventilation during induction and intubation until lung isolation is secured. This avoids the possibility of inadequate positive-pressure ventilation because of air-leak but is not well tolerated in older patients with significant comorbidity. With the availability of appropriate fiberoptic bronchoscopes, it is usually acceptable to manage patients with a normal airway using a modified rapid-sequence induction and direct bronchoscopic guidance of the DLT placement. If the patient has a postpneumonectomy fistula, the endobronchial lumen of the DLT or SLT should be placed in the noninvolved lung (i.e., for right-sided fistula a left-sided tube). Whatever anesthetic technique is used, the principle of anesthetic management for a bronchopleural fistula is: lung isolation must be confirmed before positive-pressure ventilation or repositioning the patient.

One option to avoid instrumentation of the airway in patients with bronchopleural fistula after pneumonectomy is the use of thoracic epidural anesthesia with intravenous sedation during minimally invasive surgery (discussed later in “Nonintubated Thoracic Surgery”).²⁶³ An alternative method of ventilating patients with multiple bronchopleural fistulas is the use of high-frequency oscillatory ventilation with permissive hypercapnia. This avoids barotrauma to the nonoperative lung, decreases bronchopleural fistula air-leak, and optimizes the operative outcome.²⁶⁴ The advantage of high-frequency oscillatory ventilation over conventional mechanical ventilation is that it uses lower peak airway pressure and higher minimum airway pressure and may decrease the air leak across the fistula. Early extubation in the operating room should be considered in all patients undergoing fistula repair to avoid barotrauma to the surgical stump from positive-pressure ventilation in the postoperative period.

A report of two cases described the use of venovenous ECMO in a patient with an existing left bronchopleural fistula and thoracostomy who required a right thoracotomy for tumor resection (left lung ventilation and right lung collapse).²⁶⁵ ECMO was initiated prior to OLV to maintain oxygenation during lung collapse.

Blebs, Bullae, Cysts, and Pneumatoceles

BLEBS

A bleb is a subpleural collection of air under the visceral pleura caused by a ruptured alveolus. The air dissects through the pulmonary parenchyma and enlarges to form a bubble on the surface of the lung. Blebs most commonly occur at the apices of the lung and can rupture into the interpleural space, causing a pneumothorax. A single episode of spontaneous pneumothorax is usually treated conservatively with chest tube drainage until the air leak has stopped. Resection of blebs is commonly indicated for recurrent pneumothoraces, bilateral pneumothoraces, or prolonged chest tube drainage. Resection of blebs after a single pneumothorax may be indicated if the patient's occupation exposes them to significant rapid fluctuations in atmospheric pressure (e.g., flight crews or scuba divers). Resection is most commonly combined with a procedure to obliterate the pleural space by partial pleurectomy or pleural abrasion. Resection of blebs is most often performed by VATS. Although VATS procedures per se are generally associated with a limited need for postoperative analgesia, pleurectomy or abrasion can be very painful.

BULLAE

Bullae are thin-walled, air-filled intraparenchymal lung spaces caused by the loss of alveolar structural tissue (Fig. 53.53). These are usually associated with emphysema, but

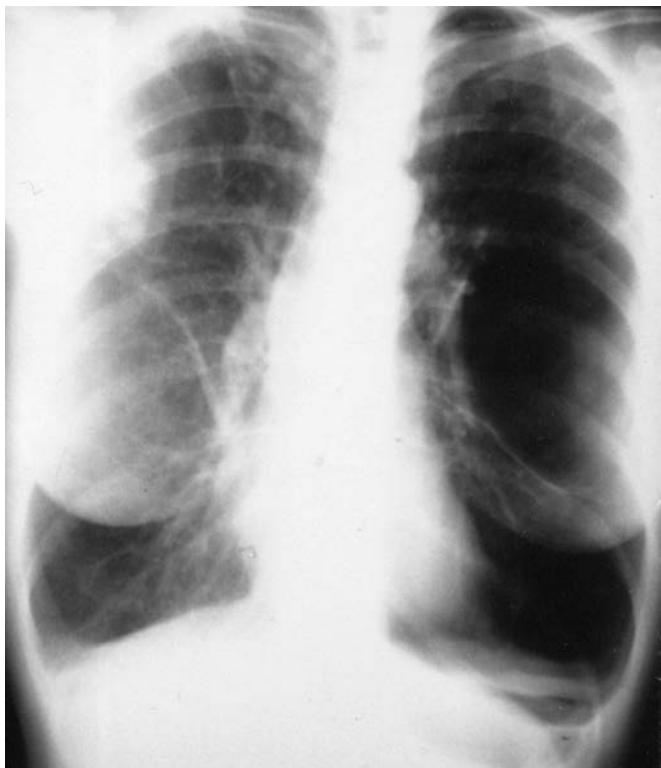


Fig. 53.53 Chest radiograph of a patient with severe emphysema and multiple bullae including giant bullae of the left upper and lower lobes. This patient also has a carcinoma of the right upper lobe.

their exact cause is unclear. Although there is some confusion over terminology in this area, bullous-like lesions of the lung associated with congenital malformations or secondary to trauma or infection are more correctly termed pneumatoceles or cysts. There are no universally accepted surgical indications for resection of lung bullae. A patient with symptomatic dyspnea and a giant bulla (or bullae) that occupies more than 30% of a hemithorax and in whom radiography and CT scans suggest that reasonably functional lung tissue can be restored to a more anatomically favorable position should be considered for bullectomy. Factors that support the effect of the bullae as a cause of a patient's dyspnea are a restrictive pattern of spirometry (proportional decrease of both FEV_1 and FVC) and a discrepancy in lung volume studies in which the FRC measured by plethysmography exceeds the FRC measured by helium dilution by more than 2 liters.

In the usual tidal volume range, bullae are more compliant than normal lung and fill preferentially during spontaneous ventilation. However, beyond the normal tidal volume range, bullae become much less compliant and the intrabulla pressure rises acutely as airway pressure increases. Measurement of *in vivo* intrabullae pressures in patients using fine needles both before and during anesthesia showed no evidence of a valve mechanism.⁶⁰ All bullae studied communicated with the central airways, although some very slowly. The typical compression pattern seen on radiographs or CT scans is most likely due to secondary elastic recoil of normal lung regions (see Fig. 53.9). Intrabulla pressure at FRC corresponds with the mean airway pressure averaged over the respiratory cycle. Thus during spontaneous ventilation, the intrabulla pressure will be negative with respect to the surrounding lung tissue. However, whenever positive pressure is used, the intrabulla pressure will rise in relation to surrounding lung regions. There is a risk of hyperinflation and rupture whenever positive pressure is used. The complications of bulla rupture can be life threatening because of hemodynamic collapse from tension pneumothorax or inadequate ventilation owing to resultant bronchopleural fistulae.

Relief of dyspnea symptoms and improved pulmonary function are well documented in patients after resection of giant bullae with most patients showing an increase in FEV_1 of more than 0.3 L and excellent short-term improvement in quality of life, but with a decrease in improvement by 3 years.²⁶⁶ Hypercapnia is not a contraindication to bullae resection. Lung infection must be meticulously treated preoperatively. Outcome depends on patient age, smoking history, and cardiac status. In the postoperative period lung air leaks are the major complication. The surgical approach can be by traditional sternotomy or by VATS. Laser resection may decrease the incidence of air leaks. Various non-surgical thoracoscopic and bronchoscopic procedures such as the subsegmental injections of fibrin glue have been used to deal with these air leaks.

The anesthetic considerations for bullectomy are similar to those for a patient with a bronchopleural fistula, with the exceptions that it is best not to place a chest drain prophylactically as this may enter the bulla and create a fistula, and there is not the risk of soiling healthy lung regions from extrapleural fluid that there is with fistulae. For induction of anesthesia it is optimal to maintain spontaneous ventilation

or to use small tidal volumes and low airway pressures until the lung or lobe with the bulla or bleb is isolated.²⁶⁷ When there is a risk of aspiration or it is felt that the patient's gas exchange or hemodynamics may not permit spontaneous ventilation for induction, the anesthesiologist will have to use small tidal volumes and low airway pressures during positive pressure ventilation until the airway is isolated.

CYSTS

Congenital bronchogenic cysts are products of abnormalities in the tracheobronchial budding process of lung organogenesis. They may occur peripherally within the lung parenchyma (70%) or centrally attached to the mediastinum or hilum. Bronchogenic cysts become problematic if they become enlarged, exerting a mass effect on functional lung or mediastinal structures; if they rupture and create a pneumothorax; or if they become infected. Small cysts without communication to a bronchus are asymptomatic and may be incidentally noted as round, clearly demarcated lesions on chest radiographs. Communicating cysts often produce air-fluid levels, are prone to recurrent infection, and may trap air by a ball-valve mechanism, risking rapid expansion or rupture. Infected cysts may be obscured by surrounding pneumonia, or they may be difficult to differentiate from an empyema. CT scans help differentiate cystic from solid lesions. Conservative surgical excision of bronchogenic cysts is generally recommended, whether or not a bronchial communication is evident.

Pulmonary hydatid cysts are watery, parasitic cysts containing larvae of the dog tapeworm, *Echinococcus granulosus*.²⁶⁸ *E. granulosus* is a relatively common cause of pulmonary cysts in endemic areas (Australia, New Zealand, South America, and some third-world regions). Hydatid cysts may grow in diameter by as much as 5 cm/year and become medically problematic in several ways. By mass effect, they may exert pressure on adjacent structures (e.g., bronchus, great vessels, esophagus). Spontaneous or traumatic rupture may occur, sending fluid, parasites, or laminated debris into adjacent tissue, bronchus, pleura, or the circulation (i.e., systemic emboli). Hypersensitivity reactions, bronchospasm, and anaphylaxis can result. Drainage into the bronchi may cause dramatic expulsion of fluid with respiratory distress or asphyxiation, depending on the amount of fluid involved. Rupture into the pleural space may result in a large hydropneumothorax, severe dyspnea, shock, suffocation, or anaphylaxis. Rupture becomes more dangerous and more likely as cysts become larger. It is recommended that any cyst larger than 7 cm should be removed.

Small, intact peripheral cysts are often easily enucleated without loss of lung parenchyma. Segmentectomy or lobectomy is indicated when single or multiple cysts occupy most of the segment or lobe. Patients with suppurative cysts should be prepared for surgery with postural drainage and antibiotics. Lung isolation and/or reduced airway pressure during dissection may be helpful in preventing herniation of the cyst. Increased airway pressure at the time of delivery may aid removal of the cyst. The multiple bronchial openings in the residual cavity must then be identified and closed. Multiple "leak tests" with saline in the residual opening may be required to locate all bronchial openings. An

alternative surgical strategy is to inject hypertonic saline into the cyst to sterilize it, followed by aspiration of the contents and removal of the evacuated cyst.

PNEUMATOCELE

Pneumatoceles are thin-walled, air-filled spaces generated by pulmonary infections or trauma. They usually appear in the first week of a pneumonia and resolve spontaneously within 6 weeks. As with other lung cysts, potential complications of pneumatoceles include secondary infection and enlargement as a result of air entrapment, with possible rupture or displacement and compression of normal lung. Adverse hemodynamic consequences may result either from a tension pneumothorax or a tension pneumatocele. The latter is unusual and is presumed to result from a one-way valve mechanism, usually in the setting of positive-pressure mechanical ventilation.²⁶⁹ Occasionally, surgical decompression is required and is performed by percutaneous needle aspiration, catheter drainage, or chest tube drainage under CT or fluoroscopic guidance. Rarely is thoracoscopic or open surgical drainage or excision required.

Lung Transplantation

End-stage pulmonary disease is one of the most common causes of death. Lung transplantation is a definitive treatment for these patients. Indications and contraindications to lung transplantation are summarized in **Box 53.15**. Approximately 1500 lung transplants are performed annually worldwide; the number is limited by the supply of donor organs. Recipients fall into four major categories (by frequency of indication):

1. Pulmonary fibrosis: idiopathic, associated with connective tissue disorders, other
2. COPD
3. Cystic fibrosis (**Fig. 53.54**) and other congenital forms of bronchiectasis
4. Primary pulmonary hypertension

There are also several other, rarer indications such as primary bronchoalveolar lung cancer, lymphangioleiomyomatosis, and so on.²⁷⁰ Depending on the patient's pathophysiology, there are several surgical options: single-lung transplantation, bilateral sequential (double) lung transplantation, heart-lung transplantation, and living-related lobar transplantation. An overall 5-year survival rate of 50% is the benchmark but depends on recipient age and diagnosis. Survival is generally better with double-lung than single-lung transplants, with the exception of elderly pulmonary fibrotic patients, for whom there is no outcome difference between the two procedures.

Anesthetic airway management is most commonly done with a DLT. The advantage of using a DLT in transplantation is that it allows direct continuous access to both lungs for suctioning, oxygenation, and examination of the bronchial anastomoses. Several advances have allowed the use of DLTs for transplantation. The use of segmental bronchial lavage at induction via an SLT, before placement of the DLT, facilitates suctioning via the DLT in patients with copious secretions. Monitoring

BOX 53.15 Indications and Contraindications for Lung Transplantation

Indications

- Untreatable end-stage pulmonary, parenchymal, and/or vascular disease
- Absence of other major medical illnesses
- Substantial limitation of daily activities
- Projected life expectancy less than 50% of 2- to 3-year predicted survival
- New York Heart Association Class III or IV functional level
- Rehabilitation potential
- Satisfactory psychosocial profile and emotional support system
- Acceptable nutritional status
- Disease-specific mortality exceeding transplant-specific mortality over 1 to 2 years

Relative Contraindications

- Over 65 years of age
- Critical or unstable clinical conditions (e.g., shock, mechanical ventilation, or extracorporeal membrane oxygenation)
- Severely limited functional status with poor rehabilitation potential
- Colonization with highly resistant or virulent bacteria, fungi, or mycobacteria
- Severe obesity defined as a body mass index greater than 30 kg/m²
- Severe or symptomatic osteoporosis
- Other medical conditions not resulting in end-organ damage (e.g., diabetes mellitus, systemic hypertension, peripheral vascular disease, gastroesophageal reflux, patients with coronary artery disease s/p coronary artery stenting or percutaneous transluminal coronary angioplasty)

Absolute Contraindications

- Untreatable advanced dysfunction of another major organ system (e.g., heart, liver, kidney)
- Active malignancy within the previous 2 years
- Noncurable chronic extrapulmonary infection
- Chronic active viral hepatitis B, hepatitis C, or HIV
- Significant chest wall or spinal deformity
- Documented nonadherence or inability to follow through with medical therapy, office follow-up, or both
- Untreatable psychiatric or psychologic condition associated with inability to cooperate or comply with medical therapy
- Absence of a consistent or reliable social support system
- Substance addiction (e.g., alcohol, tobacco, narcotics) that is either active or was active within the previous 6 months

Based on Weill D, et al. *J Heart Lung Transplant*. 2015;34:1.

includes invasive arterial and pulmonary catheters and TEE in most centers. Anesthetic maintenance is based mainly on intravenous infusions because of the frequent need for airway access (i.e., suctioning, bronchoscopy), which causes problems maintaining a stable level of inspired anesthetic vapor. In spite of advances in lung preservation techniques, it is optimal to limit the donor lung ischemic period to 4 hours.

There are wide site-specific variations in the use of ECMO and CPB during lung transplantation. For adults, intraoperative venoarterial ECMO is largely replacing CPB due to the decreased need for blood transfusions and improved postoperative outcomes.²⁷¹ Venovenous ECMO is used increasingly for postoperative respiratory support.

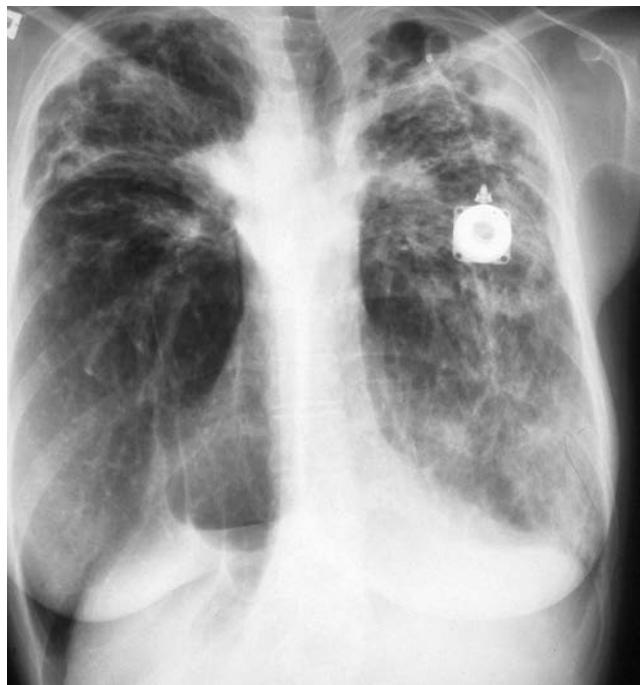


Fig. 53.54 Chest radiograph of a patient with cystic fibrosis for bilateral lung transplantation. The chest image shows a typical pattern of bronchiectasis. A subcutaneous intravenous injection reservoir is seen over the upper left chest.

The intraoperative anesthetic complications depend, in large part, on the underlying lung disease. Emphysema patients are prone to hypotension on induction from positive-pressure ventilation (see COPD in “Preoperative Evaluation of the Thoracic Surgery Patient” earlier). Problems in cystic fibrosis patients include the inability to deal with thick bronchial secretions and to adequately ventilate these patients. Cystic fibrosis patients, because they have both increased inspiratory and expiratory flow resistances, may benefit from slow inspiratory phase ventilation with a high airway pressure.²⁷² Because of the severely decreased lung compliance, this method of ventilation causes little hemodynamic compromise in this subgroup of patients, if air trapping is avoided. Other recipient disease-specific problems include: hemodynamic collapse on induction because of right-heart dysfunction in primary pulmonary hypertensives, the poor tolerance of pulmonary fibrotic patients for OLV, and the risk of pneumothoraces in patients with lymphangiomyomatosis.

ANESTHESIA FOR THE PATIENT AFTER LUNG TRANSPLANTATION

Many lung transplant recipients subsequently require anesthesia for related, or unrelated, surgical problems.²⁷³ The frequency with which they present for surgery may be caused by complications of immunosuppression (e.g., infection, tumor, renal failure) or complications of the transplantation (e.g., bronchial stenosis, bronchiolitis obliterans).

A review of the patient's prior spirometry and diffusion capacity tests should be carried out to identify patients who have low pulmonary reserve. Bronchiolitis obliterans syndrome (BOS) is a chronic rejection disorder seen in many

post-lung transplant patients that leads to a restrictive lung disease. BOS accounts for a considerable proportion of the deterioration in lung function and affects more than half of the recipients that survive beyond 5 years. It is the main cause of mortality in patients who survive more than a year.²⁷⁴

Most transplant recipients can be managed according to routine anesthetic practice including optimal perioperative respiratory care, antibiotic prophylaxis, and maintenance of immune suppression. Results of recent blood gas analysis, chest radiographs, and CT scans are vital in managing these patients. Most adults will have bronchial anastomoses and there will be no problem with endotracheal intubation. If endobronchial intubation or a DLT is used, a bronchoscopy should be performed first to assess the bronchial anastomoses, and the intubation should be with fiberoptic guidance.

Single-lung transplant recipients with native lung emphysema are a specific concern. They have a marked imbalance in pulmonary compliance, with the native lung highly compliant and the donor lung of normal or reduced (if there is rejection) compliance. However, the major proportion of the pulmonary blood flow is usually to the allograft. With standard methods of positive pressure ventilation they may develop dynamic hyperinflation of the emphysematous lung with hemodynamic instability and problems with gas exchange. These patients may require the use of a DLT and independent lung ventilation techniques, reducing the airway pressure and minute ventilation in the native lung, if positive pressure ventilation is required.

LUNG VOLUME REDUCTION

The use of multiple wedge resections can reduce lung volume and improve symptoms in selected severe emphysema patients.²⁷⁵ Depending on the patient and center, this procedure may be unilateral or bilateral and performed by thoracotomy, sternotomy, or VATS. The surgery is more effective in patients with heterogeneous lung disease where the most severely affected areas (often apical) can be resected, than in patients with homogenous types of emphysema (e.g., Alpha-1 antitrypsin deficiency). Patients with extremely severe disease (FEV₁ or DLCO < 20% predicted) have poor survival after surgery.²⁷⁶ This procedure is now most commonly seen as an option for patients with severe emphysema who have contraindications to transplantation.

Immediate postoperative improvements in symptoms and pulmonary function are common, and many patients are able to discontinue or reduce home oxygen therapy. These changes are the result of a decompression of the airways and a reduction of airflow resistance and work of breathing,²⁷⁷ which results in a dramatic fall in auto-PEEP (intrinsic PEEP) with a corresponding increase in dynamic compliance. Despite the encouraging changes in early postoperative pulmonary function, the improvement in respiratory function as a result of this surgery is transient.²⁷⁸ However, this must be viewed in the context of the short life expectancy of patients with this degree of emphysema and the potential for improvement in their quality of life from the operation.

Anesthetic management is similar to that for other patients with severe COPD having thoracic surgery (see COPD in “Preoperative Evaluation of the Thoracic Surgery

Patient” earlier) with the risk of hypotension on induction caused by auto-PEEP and the need for excellent analgesia to avoid postoperative mechanical ventilation.²⁷⁹ This procedure is now performed in some centers using one-way valves or coils placed bronchoscopically in the most involved segments to cause collapse of severely emphysematous distal lung regions,²⁸⁰ thus avoiding surgery.

Pulmonary Hemorrhage

Massive hemoptysis is defined as expectoration of more than 200 mL of blood in 24 to 48 hours. The most prevalent causes are carcinoma, bronchiectasis, and trauma (e.g., blunt, penetrating, or secondary to a pulmonary artery catheter). Death can occur quickly as a result of asphyxia. Management requires four sequential steps: lung isolation, resuscitation, diagnosis, and definitive treatment. The anesthesiologist is often called to deal with these cases outside of the operating room. There is no consensus on the best method of lung isolation for these cases. The initial method for lung isolation will depend on the availability of appropriate equipment and an assessment of the patient’s airway. All three basic methods of lung isolation have been used: DLTs, SLTs, and bronchial blockers. Fiberoptic bronchoscopy is usually not helpful to position endobronchial tubes or blockers in the presence of torrential pulmonary hemorrhage and lung isolation must be guided by clinical signs (primarily auscultation). DLTs will achieve rapid and secure lung isolation. Even if a left-sided tube enters the right mainstem bronchus, only the right upper lobe will be obstructed. However, suctioning large amounts of blood or clots is difficult through the narrow lumens of a DLT. An option is initial placement of an SLT for oxygenation and suctioning then replacement with a DLT either by laryngoscopy or with an appropriate tube exchanger. An uncut single-lumen ETT can be advanced directly into the right mainstem bronchus or rotated 90 degrees counterclockwise for advancement into the left mainstem bronchus.²⁸¹ A bronchial blocker will normally pass easily into the right mainstem bronchus and is useful for right-sided hemorrhage (90% of pulmonary artery catheter-induced hemorrhages are right-sided). Except for cases with blunt or penetrating trauma, after lung isolation and resuscitation have been achieved, diagnosis and definitive therapy of massive hemoptysis are now most commonly performed by coiling of the pulmonary artery false aneurysm in invasive radiology.²⁸²

PULMONARY ARTERY CATHETER-INDUCED HEMORRHAGE

Hemoptysis in a patient with a pulmonary artery catheter must be assumed to be caused by perforation of a pulmonary vessel by the catheter until proven otherwise. The mortality rate may exceed 50%. This complication seems to be occurring less than previously, possibly related to stricter indications for the use of pulmonary artery catheters and more appropriate management of the catheters with less reliance on wedge measurements. Therapy for pulmonary artery catheter-induced hemorrhage should follow an organized protocol with some variation depending on the severity of the hemorrhage (Box 53.16).

BOX 53.16 Management of the Patient With a Pulmonary Artery Catheter

Induced Pulmonary Hemorrhage

- Initially position the patient with the bleeding lung dependent.
- Perform endotracheal intubation, oxygenation, airway toilet.
- Isolate the lung by endobronchial double- or single-lumen tube or bronchial blocker.
- Withdraw the pulmonary artery catheter several centimeters, leaving it in the main pulmonary artery. Do not inflate the balloon (except with fluoroscopic guidance).
- Position the patient with the isolated bleeding lung nondependent. Administer positive end-expiratory pressure to the bleeding lung if possible.
- Transport the patient to medical imaging for diagnosis and embolization if feasible.

During Weaning from Cardiopulmonary Bypass

Weaning from CPB is one of the times when pulmonary artery catheter-induced hemorrhage is most likely to occur. Management of the pulmonary artery catheter during CPB by withdrawal from a potential wedge depth and observing the pulmonary artery pressure waveform to avoid wedging during CPB may decrease the risk of this complication. When hemoptysis occurs during CPB weaning, the anesthesiologist should resist the temptation to rapidly reverse the anticoagulation in order to quickly discontinue CPB, because this can lead to fatal asphyxiation from hemorrhage. Resumption of full CPB ensures oxygenation while the tracheobronchial tree is suctioned and then visualized with fiberoptic bronchoscopy. The use of a pulmonary artery vent may be required to decrease the pulmonary blood flow sufficiently to define the bleeding site (usually the right lower lobe). The pleural cavity should be opened to assess the lung parenchymal damage. Conservative management with lung isolation, to avoid lung resection, is optimal therapy if possible. In patients with persistent hemorrhage who are not candidates for lung resection, temporary lobar pulmonary artery occlusion with a vascular loop during and after weaning from CPB may be an option.

Posttracheostomy Hemorrhage

Hemorrhage in the immediate postoperative period following a tracheostomy is usually from local vessels in the incision such as the anterior jugular or inferior thyroid veins. Massive hemorrhage 1 to 6 weeks postoperatively is most commonly caused by tracheoinnominate artery fistula.²⁸³ A small sentinel bleed occurs in most patients before a massive bleed. The management protocol for tracheoinnominate artery fistula is outlined in [Box 53.17](#).

Pulmonary Thromboendarterectomy

Pulmonary thromboendarterectomy is a potentially curative procedure for chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is a progressive disorder that responds poorly to conservative therapy, and pulmonary thromboendarterectomy is the most appropriate treatment, with a perioperative mortality of approximately 4%,

BOX 53.17 Management of Tracheoinnominate Artery Fistula Hemorrhage

- Overinflate the tracheostomy cuff to tamponade the hemorrhage.
- If this fails:
 - Replace the tracheostomy tube with an oral endotracheal tube. Position the cuff with fiberoptic bronchoscopic guidance just above the carina.
 - Apply digital compression of the innominate artery against the posterior sternum using a finger passed through the tracheostomy stoma.
- If this fails:
 - Slowly withdraw the endotracheal tube and overinflate the cuff to tamponade.
 - Proceed with definitive therapy: sternotomy and ligation of the innominate artery.

which is less than lung transplantation. The majority of patients with CTEPH present for medical evaluation late in the disease because many have not had an obvious episode of deep venous thrombosis or pulmonary embolus, and the progression of the disease is insidious. Patients present with severe dyspnea on exertion and signs of right-sided heart failure. Surgical candidates have hemodynamically significant pulmonary vascular obstruction (pulmonary vascular resistance >300 dynes/sec/cm⁵), with potentially accessible proximal areas of thromboemboli.

An inferior vena cava filter is often placed prophylactically prior to surgery. Surgery is performed via a midline sternotomy with CPB with or without periods of deep hypothermic circulatory arrest (DHCA). Anesthetic management is essentially the same as for a patient with primary pulmonary hypertension for lung transplantation, with the exception that there is no need for lung isolation, so airway management is done with a standard ETT. Monitoring includes femoral and pulmonary artery catheters, TEE, processed electroencephalography, and rectal/bladder temperatures.²⁸⁴

These patients are at risk of hemodynamic collapse because of right ventricular failure from hypotension during induction of general anesthesia. Induction may be performed with etomidate or ketamine to avoid hypotension. Support of SVR with noradrenaline or phenylephrine is usually required. If DHCA is used, it is preceded by mannitol and methylprednisolone to try to decrease cerebral cellular edema and to improve free-radical scavenging. The speed of warming and cooling is controlled on CPB to maintain a temperature gradient less than 10°C between blood and bladder/rectal temperatures. Periods of DHCA are usually limited to 20 minutes. Massive pulmonary hemorrhage occurs rarely during CPB in these cases. The instillation of phenylephrine 10 mg and vasopressin 20 units diluted in 10 mL saline via the ETT may be beneficial. Postoperatively, the patients are kept sedated, intubated, and ventilated for at least 24 hours to decrease the risk of reperfusion pulmonary edema. Noradrenaline or vasopressin infusions may be used to elevate the SVR and decrease cardiac output in order to decrease pulmonary blood flow.

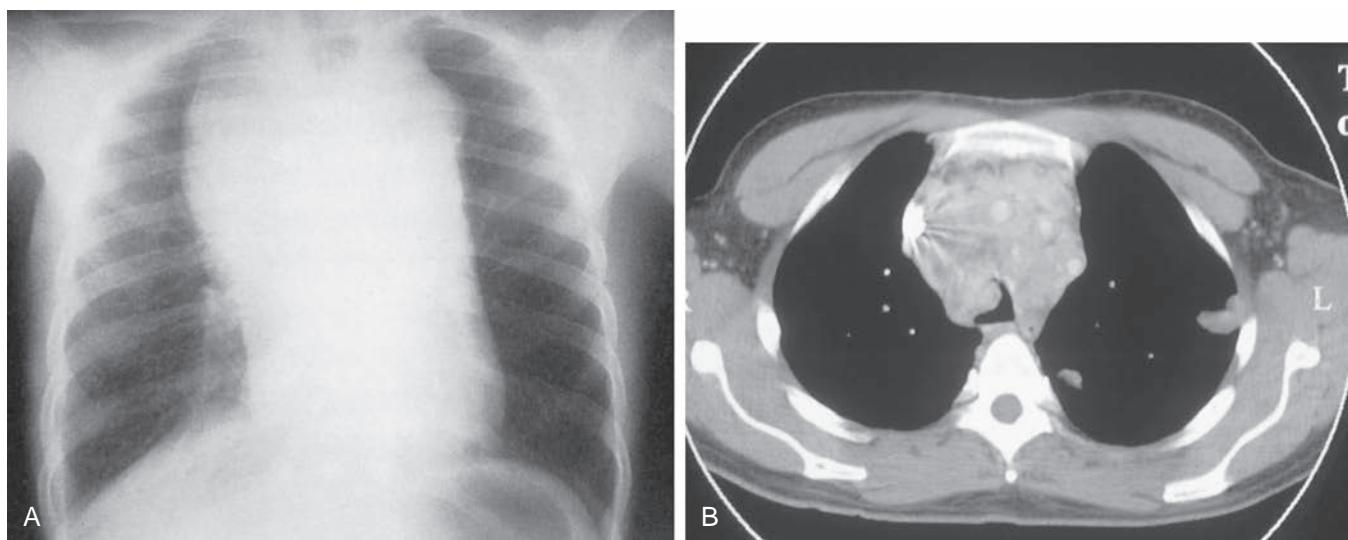


Fig. 53.55 (A) Chest radiograph of an adult patient with an anterosuperior mediastinal mass. This mass was a lymphoma. (B) A thoracic computed tomographic scan with contrast just above the level of the carina shows partial compression of the carina and right mainstem bronchus. This patient has an "Uncertain" distal airway (see text).

Bronchopulmonary Lavage

Bronchopulmonary lavage (BPL) is a treatment during which up to 10 to 20 L of normal saline are instilled then drained in 500- to 1000-mL aliquots through one side of a DLT into one lung under general anesthesia until the effluent is clear.²⁸⁵ It may then be performed on the contralateral lung during the same anesthetic or during a subsequent anesthetic after a period of several days for recovery. It is the most effective treatment modality for symptomatic pulmonary alveolar proteinosis. This lung disease results from accumulation in the alveoli of a lipoprotein material similar to surfactant.²⁸⁶ This disease seems to have an immune component, and some patients respond to conservative medical therapy with granulocyte-macrophage colony-stimulating factor.²⁸⁷ Other pathologic states that have been treated by BPL include cystic fibrosis, asthma, radioactive dust inhalation, lipoid pneumonitis, and silicosis, all without convincing success.

General anesthesia is induced and maintained with intravenous infusions as for lung transplantation. Airway management is with a left-sided DLT.²⁸⁸ The patient is kept in the supine position during the procedure. Because of transmitted hydrostatic pressure from the lavage lung to the pulmonary circulation, oxygenation increases during the filling phase and decreases during the emptying phase in synchrony with changes in the pulmonary blood flow distribution. These changes are usually transient and well tolerated. Usually 10 to 15 L is instilled and more than 90% is recovered leaving a deficit of less than 10%. At the end of the procedure, the lavaged lung is thoroughly suctioned. A dose of furosemide (10 mg) is administered to increase diuresis of absorbed saline. If the plan is to proceed to a lavage of the contralateral lung, there is a period of at least 1 hour of TLV to allow recovery of the lavaged lung, during which arterial blood gases are monitored. If there is a persistent large alveolar-arterial oxygen gradient preventing lavage of the second lung, venovenous ECMO may be instituted or the patient can be brought back for lavage of the

other lung at a later date. Postprocedure, after reintubation with an SLT, a fiberoptic bronchoscopic inspection is performed for suctioning. Conventional ventilation with PEEP is continued, usually for less than 2 hours. Observation in the intensive care unit for 24 hours is part of the routine procedure. Some patients require lavage every few months, whereas others remain in remission for years.

Mediastinal Masses

Patients with mediastinal masses, particularly masses in the anterior or superior mediastinum, or both, present unique problems for the anesthesiologist. Patients may require anesthesia for biopsy of these masses by mediastinoscopy or VATS, or they may require definitive resection via sternotomy or thoracotomy. Tumors of the mediastinum include thymoma, teratoma, lymphoma, cystic hygroma, bronchogenic cyst, and thyroid tumors. Mediastinal masses may cause obstruction of major airways, main pulmonary arteries, atria, and the superior vena cava. During induction of general anesthesia in patients with an anterior or superior mediastinal mass, airway obstruction is the most common and feared complication. It is important to note that the point of tracheobronchial compression usually occurs distal to an ETT (Fig. 53.55) and it may not be possible to forcibly pass an ETT through the airway once it has collapsed. A history of supine dyspnea or cough should alert the clinician to the possibility of airway obstruction upon induction of anesthesia. Life-threatening complications may occur in the absence of symptoms in children. The other major complication is cardiovascular collapse secondary to compression of the heart or major vessels. Symptoms of supine presyncope suggest vascular compression.

Anesthetic deaths have mainly been reported in children. These deaths may be the result of the more compressible cartilaginous structure of the airway in children or because of the difficulty in obtaining a history of positional symptoms in children. The most important diagnostic test in the

patient with a mediastinal mass is the CT scan of the trachea and chest. Children with tracheobronchial compression greater than 50% on CT scan cannot be safely given general anesthesia.²⁸⁹ Flow-volume loops, specifically the exacerbation of a variable intrathoracic obstructive pattern (expiratory plateau) when supine, are unreliable²⁹⁰ for predicting which patients will have intraoperative airway collapse.²⁹¹ Transthoracic echocardiography is indicated for patients with vascular compression symptoms.

MANAGEMENT

General anesthesia will exacerbate extrinsic intrathoracic airway compression in three ways. First, reduced lung volume occurs during general anesthesia and tracheobronchial diameters decrease according to lung volume. Second, bronchial smooth muscle relaxes during general anesthesia allowing greater compressibility of large airways. And third, paralysis eliminates the caudal movement of the diaphragm seen during spontaneous ventilation. This eliminates the normal transpleural pressure gradient that dilates the airways during inspiration and minimizes the effects of extrinsic intrathoracic airway compression.

Management of these patients is guided by their symptoms and the CT scan (Boxes 53.18 and 53.19). Patients with “uncertain” airways should have diagnostic procedures performed under local or regional anesthesia whenever possible. Patients with “uncertain” airways requiring general anesthesia need a step-by-step induction of anesthesia with continuous monitoring of gas exchange and

BOX 53.18 Grading Scale for Symptoms in Patients With an Anterior or Superior Mediastinal Mass

Asymptomatic
Mild: Can lie supine with some cough/pressure sensation
Moderate: Can lie supine for short periods but not indefinitely
Severe: Cannot tolerate supine position

BOX 53.19 Stratification of Patients with Mediastinal Masses Regarding Safety for General Anesthesia

- | | | |
|---------------------|-------|---|
| A. Safe | (I) | Asymptomatic adult, CT minimal tracheal/bronchial diameter >50% of normal |
| B. Unsafe | (I) | Severely symptomatic adult or child |
| | (II) | Children with CT tracheal/bronchial diameter <50% of normal, regardless of symptoms |
| C. Uncertain | (I) | Mild/moderate symptomatic child with CT tracheal/bronchial diameter >50% of normal |
| | (II) | Mild/moderate symptomatic adult with CT tracheal/bronchial diameter <50% of normal |
| | (III) | Adult or child unable to give history |

CT, Computed tomography scan.

hemodynamics. This “NPIC” (*noli pontes ignii consumere*; i.e., “don’t burn your bridges”) anesthetic induction can be an inhalation induction with a volatile anesthetic such as sevoflurane or intravenous titration of propofol with or without ketamine, maintaining spontaneous ventilation until either the airway is definitively secured or the procedure is completed.²⁹² Awake intubation of the trachea before induction is a possibility in some adult patients if the CT scan shows an area of noncompressed distal trachea to which the ETT can be advanced before induction. If muscle relaxants are required, ventilation should first be gradually taken over manually to assure that positive-pressure ventilation is possible and only then can a short-acting muscle relaxant be administered (Box 53.20).

Development of airway or vascular compression requires that the patient be awakened as rapidly as possible and then other options for the procedure be explored. Intraoperative life-threatening airway compression usually responds to one of two therapies: either repositioning of the patient (it must be determined before induction if there is a position that causes less compression and less symptoms) or rigid bronchoscopy and ventilation distal to the obstruction (this means that an experienced bronchoscopist and equipment must always be immediately available in the operating room for these cases). The rigid bronchoscope, even if passed into only one mainstem bronchus, can be used for oxygenation during resuscitation (see “Rigid Bronchoscopy,” earlier).²⁹³ Once adequate oxygenation has been restored the rigid bronchoscope can be used to position an airway exchange catheter, over which an ETT is passed after the bronchoscope is withdrawn. An alternative technique to secure the airway with rigid bronchoscopy is to first mount an ETT over a small rigid bronchoscope (e.g., 6 mm) and then perform rigid bronchoscopy using the bronchoscope to deliver the ETT distal to the obstruction.²⁹⁴

Institution of femorofemoral ECMO before induction of anesthesia is a possibility for some adult patients who are “unsafe” for NPIC general anesthesia. The concept of CPB “standby” during attempted induction of anesthesia is fraught with danger²⁹⁵ because there is not enough time after a sudden airway collapse to establish CPB before hypoxic cerebral injury occurs.²⁹⁶ Other options for “unsafe” patients include local anesthetic biopsy of the mediastinal mass or biopsy of another node (e.g., supraclavicular), preoperative radiotherapy with a nonradiated “window” for subsequent biopsy, preoperative chemotherapy or short-course steroids, and CT-guided biopsy of mass or drainage

BOX 53.20 Management for All Patients With a Mediastinal Mass and an Uncertain Airway for General Anesthesia

1. Determine optimal positioning of patient preoperatively
2. Secure airway beyond stenosis when patient is awake, if feasible
3. Have rigid bronchoscope and surgeon available at induction of anesthesia
4. Maintain spontaneous ventilation if possible (*noli pontes ignii consumere*)
5. Monitor for airway compromise postoperatively

of a cyst. The salient points in managing a patient with an anterior or superior mediastinal mass include²⁹⁷:

1. In virtually all children and adults with a mediastinal mass, diagnostic procedures and imaging can be performed, if necessary, without subjecting the patient to the risks of general anesthesia.²⁹⁸
2. An extrathoracic source of tissue for diagnostic biopsy (pleural effusion or extrathoracic lymph node) should be sought as an initial measure in every patient.
3. Regardless of the proposed diagnostic or therapeutic procedure, the flat, supine position is never mandatory.
4. In the high-risk child (Box 53.21) without extrathoracic lymphadenopathy or a pleural effusion, prebiopsy steroid therapy is justifiable.²⁹⁹ In this case, coordination with oncology, surgery, and anesthesiology is essential to organize timing of the biopsy. An alternative to preoperative steroids in the cooperative high-risk patient includes irradiating the tumor while leaving a small area covered with lead for subsequent biopsy.

With improved awareness of the risk of acute intraoperative airway obstruction in these patients, life-threatening events are now less likely to occur in the operating room. In children these events now tend to occur preoperatively if the patient is forced to assume a supine position for imaging. In adults, acute airway obstruction is now more likely to occur postoperatively in the recovery room.³⁰⁰ Vigilance must be maintained throughout the entire perioperative period.

Thymectomy for Myasthenia Gravis

Myasthenia gravis is a disease of the neuromuscular junction; affected patients have weakness caused by a decreased number of acetylcholine receptors at the motor endplate.³⁰¹ Patients may or may not have an associated thymoma. Thymectomy is frequently performed to induce clinical remission, even in the absence of a thymoma. The effects of muscle relaxants are modified by this disease; myasthenic patients are resistant to succinylcholine and extremely sensitive to nondepolarizing blockers. Thymectomy may be performed via full or partial sternotomy, or with a minimally invasive approach via a transcervical incision or VATS. For thymectomy with a thymoma, a sternotomy is used. In the absence of an identifiable tumor, minimally invasive techniques are commonly used. Ideally, the use of neuromuscular relaxation is avoided. Induction of anesthesia with propofol, remifentanil, and topical anesthesia of the airway

BOX 53.21 Predictors of Airway Compromise in Children With a Mediastinal Mass

1. Anterior location
2. Histological diagnosis of lymphoma
3. Superior vena cava syndrome
4. Radiologic evidence of major vessel compression or displacement
5. Pericardial or pleural effusion

Based on Lam JCM, et al. *Pediatr Surg Int*. 2004;20:180.

facilitates intubation without the use of muscle relaxants. Alternatively, inhalational induction with a halogenated agent such as sevoflurane may be performed.³⁰² For sternotomy, combined general and thoracic epidural anesthesia is a useful technique.

Neuromuscular blockers should be used with caution in myasthenic patients because of the increased sensitivity to nondepolarizing muscle relaxants that might result in prolonged postoperative partial paralysis associated with increased morbidity and the need for postoperative mechanical ventilation.³⁰³ The cyclodextrin derivative, Sugammadex, encapsulates steroid neuromuscular blocking agents. Sugammadex has been approved as a therapy for reversal of neuromuscular blockade induced by the steroid nondepolarizing neuromuscular blocking drugs, rocuronium and vecuronium. Sugammadex is used to reverse rocuronium in myasthenics.³⁰⁴ Sugammadex dosing is dictated by the train-of-four response using a neuromuscular blockade monitor.

Most patients take pyridostigmine, an oral anticholinesterase, and many patients are on immunosuppressive medication (e.g., corticosteroids). On the day of surgery, pyridostigmine dosing should ensure that the patient's usual regimen is provided during the immediate perioperative period. A few patients require intravenous dosing with neostigmine until they are able to resume oral intake of pyridostigmine. A scoring system was devised for prediction of the need for prolonged mechanical ventilation after thymectomy via sternotomy.³⁰⁵ Among the criteria that contributed to the predicted need for support were disease duration longer than 6 years, chronic respiratory illness, pyridostigmine dosage greater than 750 mg/day, and vital capacity less than 2.9 L. The relevance of this score has diminished with better preoperative preparation and minimally invasive surgery.³⁰⁶ Referral for surgery early in the course of the disease and stabilization of symptoms with corticosteroids, intravenous immunoglobulin and plasmaapheresis, combined with the increased use of minimally invasive approaches, have made the need for postoperative ventilation infrequent. In optimized patients, mean hospital length of stay can be reduced to 1 day after minimally invasive, and 3 days after transsternal thymectomy.³⁰⁷ Patients should remain on their full medical regimen postoperatively. The remission from myasthenia gravis after thymectomy occurs slowly over a period of months to years.

NONINTUBATED THORACIC SURGERY

During the original thoracic surgery procedures in the late 1800s, patients were anesthetized with ether and breathed spontaneously without intubation. During open thoracotomy without oxygen supplementation, this led to progressive hypoxemia and hypercapnia and limited the duration of safe surgery. With improvements in anesthesia and VATS there has been a trend to return to nonintubated thoracic surgery in some centers. Initial reports focused on pleural drainage, lung biopsies, drainage of empyema, and similar procedures.³⁰⁸ More recently the use of nonintubated surgery has expanded to lobectomy, segmentectomy, and other more complex operations. Benefits may include shorter hospital stays and fewer postoperative complications.³⁰⁹

Techniques of nonintubated thoracic anesthesia include a variety of methods of sedation or general anesthesia that

maintain spontaneous ventilation.³¹⁰ Patients should receive supplemental oxygen to avoid hypoxemia. Patients may develop hypercapnia; however, mild hypercapnia is usually well tolerated. For patients who are hypercapnic at rest, the use of high-flow nasal oxygen may be beneficial. Dexmedetomidine provides satisfactory sedation in combination with epidural anesthesia for VATS in patients with severe respiratory dysfunction. If general anesthesia is selected, with either total intravenous or volatile anesthesia, an LMA is useful for nonintubated procedures. Regional anesthesia is commonly provided by either intercostal, paravertebral, or epidural blocks. Either of two ultrasound-guided chest wall blocks (serratus anterior plane and erector spinae plane [ESP]) (see later) may be appropriate in some patients. A remifentanil infusion may be helpful in patients who are tachypneic without hypoxemia. Also, remifentanil may decrease the cough reflex. But the risk of apnea must be appreciated and ventilation closely monitored. For surgical procedures that involve manipulation near the hilum, coughing may be problematic. Chen and associates describe the use of an intrathoracic vagal block with 2 to 3 mL of 0.25% bupivacaine injected close to the vagus nerve at the level of the lower trachea in the right hemithorax or in the aortopulmonary window on the left. This resulted in abolition of coughing for 3 hours.³¹¹

EXTRACORPOREAL MEMBRANE OXYGENATION

There is an increasing use of ECMO to manage oxygenation in thoracic surgery. ECMO has a well-established role in lung transplantation. There have been an increasing number of case reports of ECMO being used to manage oxygenation during other types of thoracic surgery where oxygenation cannot be maintained with conventional techniques.³¹² The advantage of utilizing ECMO includes the ability to maintain oxygenation and carbon dioxide removal in cases where proper ventilation is not feasible or sufficient because of patient-specific comorbidities or anatomic derangements. There are multiple reports and case series describing the use of ECMO in patients with critical airway obstruction undergoing tracheal mass removal or stenting.³¹³ Also, ECMO has been used in patients with poor gas exchange when lung collapse was required. In these reports, elective initiation of ECMO (usually venovenous) prior to induction of anesthesia or prior to the start of the procedure led to acceptable outcomes.³¹⁴ A list of potential indications for ECMO in thoracic surgery is included in **Box 53.22**. Venovenous ECMO can be performed via a single double-lumen cannula (right internal jugular) or two cannulae (usually femoral and jugular). Venoarterial ECMO can be performed with peripheral cannulation (femoral) or central cannulation (e.g., right atrium and ascending aorta). It is useful to monitor cerebral oxygen saturation in addition to peripheral saturation when ECMO is used during surgery.

Postoperative Management

ENHANCED RECOVERY AFTER SURGERY

Enhanced recovery after surgery (ERAS) is a combined multispecialty approach to perioperative management that has been adopted by many surgical specialties.³¹⁵ The concept

BOX 53.22 Potential Indications for Extracorporeal Membrane Oxygenation to Improve Oxygenation During Thoracic Surgery

- Severe airway obstruction
- Emergency loss of airway
- Extended carinal pneumonectomy
- Severe emphysema undergoing lung volume reduction surgery
- Acute respiratory distress syndrome undergoing thoracotomy and decortication
- Tracheoesophageal fistula repair after previous pneumonectomy
- Esophagectomy after previous pneumonectomy
- Segmentectomy after previous contralateral pneumonectomy
- Thoracotomy after previous single lung transplantation
- Thoracotomy with existing contralateral bronchopleural fistula
- Salvage therapy for severe chest trauma

TABLE 53.12 Surgical Modifiable Factors for Enhanced Recovery

Surgical Factor	Evidence Level	Recommendation Grade
Nutritional supplements if malnourished	Moderate	Strong
Smoking cessation	High	Strong
Pulmonary rehabilitation for borderline lung function or exercise capacity	Low	Strong
Mechanical and pharmacologic VTE prophylaxis	Moderate	Strong
Antibiotic prophylaxis	High	Strong
VATS for early stage lung cancer	High	Strong
Postoperative incentive spirometry	Low	Strong

VATS, Video-assisted thoracoscopic surgery.

Based on Batchelor T, Rasbun N, Abdelnour-Berchtold E, et al. *Eur J Cardio-Thorac Surg*. 2018, in press.

is to mitigate the stress response to surgery and enable a faster recovery. ERAS pathways in lung cancer surgery are associated with reduced complications, a shorter length of stay, and cost savings.³¹⁶ A recent panel convened by the European Society of Thoracic Surgeons has published guidelines for ERAS in thoracic surgery (**Tables 53.12 and 53.13**)³¹⁷ with suggestions for both surgical and anesthetic management. Their recommendations (strong or weak) are based on the quality of the evidence (high, moderate, low, and very low) and also the balance between desirable and undesirable effects of each intervention.

EARLY MAJOR COMPLICATIONS

There are multiple potential major complications that can occur in the immediate postoperative period following thoracic surgery, such as torsion of a remaining lobe after lobectomy, dehiscence of a bronchial stump, or hemorrhage from

TABLE 53.13 Anesthetic Modifiable Factors for Enhanced Recovery

Anesthetic Factor	Evidence Level	Recommendation Grade
Double-lumen tube or bronchial blocker for lung isolation	Moderate	Strong
Lung protective ventilation	Moderate	Strong
Temperature monitoring and active warming	High	Strong
Combined regional and general anesthesia	Low	Strong
Multimodal management of postoperative nausea and vomiting	Moderate	Strong
Inclusion of acetaminophen and nonsteroidal antiinflammatory drugs in analgesia	High	Strong
Euvolemic fluid management	High	Strong
Nonintubated thoracic surgery	Low	Not Recommended

Based on Batchelor T, Rasburn N, Abdelnour-Berchtold E, et al. *Eur J Cardio-Thorac Surg*. 2018, in press.

a major vessel. Fortunately, these are infrequent and when they do occur, the principles of management are as outlined earlier for common and specific procedures. Among the possible complications, two will be discussed in more detail: (1) respiratory failure, because it is the most common cause of major morbidity after thoracic surgery; and (2) cardiac herniation because, although it is rare, it is usually fatal if it is not quickly diagnosed and appropriately treated.

Respiratory Failure

Respiratory failure is a leading cause of postoperative morbidity and mortality in patients undergoing major lung resection. Acute respiratory failure after lung resection is defined as the acute onset of hypoxemia ($\text{PaO}_2 < 60 \text{ mm Hg}$) or hypercapnia ($\text{PaCO}_2 > 45 \text{ mm Hg}$) or the use of postoperative mechanical ventilation for more than 24 hours or reintubation for controlled ventilation after extubation. The incidence of respiratory failure after lung resection is between 2% and 18%. Patients with decreased respiratory function preoperatively are at increased risk of postoperative respiratory complications. In addition, age, the presence of coronary artery disease, and the extent of lung resection play major roles in predicting postoperative mortality and morbidity. Crossover contamination, because of the failure of lung isolation intraoperatively during lung resection in patients with contaminated secretions, can result in contralateral pneumonia and postoperative respiratory failure.³¹⁸ Mechanical ventilation during the postoperative period after lung resection is associated with the risk of acquired nosocomial pneumonia and bronchopleural fistula.

Decreased pulmonary complications in high-risk patients are associated with the use of thoracic epidural analgesia during the perioperative period.² The prevention of atelectasis and secondary infections have been attributed to better preservation of the functional RV, efficient mucociliary

clearance, and alleviation of the inhibiting reflexes acting on the diaphragm in patients receiving epidural analgesia.³¹⁹ Chest physiotherapy, incentive spirometry, and early ambulation are crucial in order to minimize pulmonary complications after lung resection. For an uncomplicated lung resection, early extubation is desirable to avoid potential complications that can arise as a result of prolonged intubation and mechanical ventilation. Current therapy to treat acute respiratory failure is supportive therapy attempting to provide better oxygenation, treat infection, and provide vital organ support without further damaging the lungs.

Cardiac Herniation

Acute cardiac herniation is an infrequent but well-described complication of pneumonectomy, where the pericardium is incompletely closed or the closure breaks down.³²⁰ It usually occurs immediately or within 24 hours after chest surgery and is associated with greater than 50% mortality. Cardiac herniation may also occur after a lobar resection with pericardial opening, or in other chest tumor resections involving the pericardium or in trauma.³²¹ When cardiac herniation occurs after a right pneumonectomy, the clinical presentation is caused by impairment of the venous return to the heart with a concomitant increase in CVP, tachycardia, profound hypotension, and shock. An acute superior vena cava syndrome ensues because of the torsion of the heart.³²² In contrast, when the cardiac herniation occurs after a left-sided pneumonectomy, there is less cardiac rotation, but the edge of the pericardium compresses the myocardium. This may lead to myocardial ischemia, the development of arrhythmias, and ventricular outflow tract obstruction. Cardiac herniation occurs after chest closure because of the pressure difference between the two hemithoraces. This pressure difference may result in the heart being extruded through a pericardial defect.

Management for a patient with a cardiac herniation should be considered as dire emergent surgery. The differential diagnosis should include massive intrathoracic hemorrhage, pulmonary embolism, or mediastinal shift from improper chest drain management. Early diagnosis and immediate surgical treatment by relocation of the heart to its anatomic position with repair of the pericardial defect or by the use of analogous or prosthetic patch material is key to patient survival. Because these patients have undergone a previous thoracotomy, all precautions should be taken for a “redo” exploration. This includes the use of large-bore intravenous catheters and an arterial line. Maneuvers to minimize the cardiovascular effects include positioning the patient in the full lateral position with the operated side up. Because time is crucial an SLT is used. Vasopressors or inotropes, or both, are required to support the circulation while exploration takes place. The use of TEE intraoperatively and after resuscitation and relocation of the heart can be considered during pericardial patch repair to prevent excessive compression of the heart by the repair.³²³ In general, patients undergoing an emergency thoracic reexploration remain intubated and are transferred to the intensive care unit postoperatively.

Postoperative Analgesia

Studies prior to 1990 consistently reported a 15% to 20% rate of major respiratory complications (atelectasis, pneumonia, respiratory failure) within the first 3 days

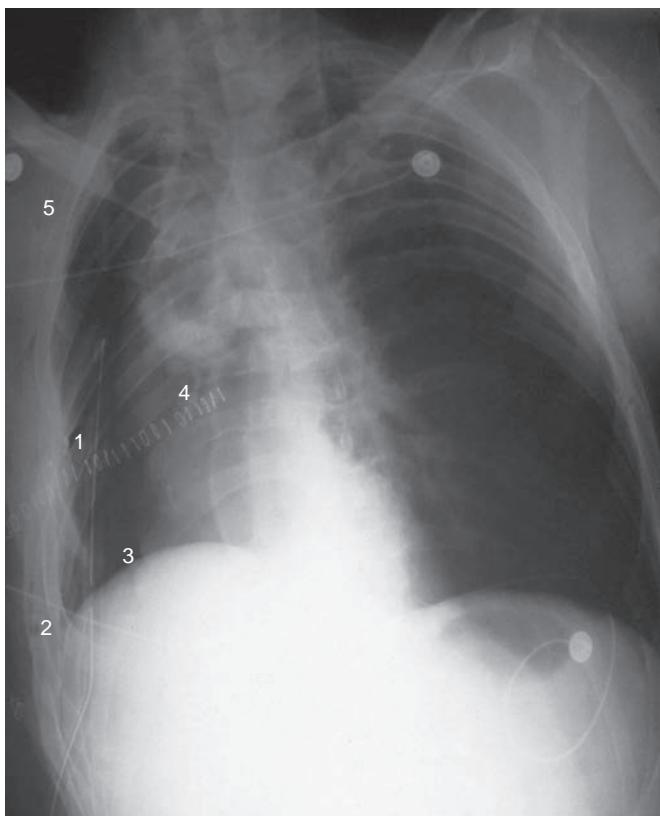


Fig. 53.56 Multiple sources of afferent transmission of pain sensations after thoracotomy. (1) Intercostal nerves at the site of the incision (usually T4-T6); (2) intercostal nerves at the site of chest drains (usually T7-T8); (3) phrenic nerve afferents from the dome of the diaphragm; (4) vagal nerve innervation of the mediastinal pleura; (5) brachial plexus.

after thoracic surgery.¹ This time of onset may relate to the unique pattern of recovery of pulmonary function following thoracotomy, which shows a delay in the initial 72-hour postoperative period that is not seen with other major surgical incisions.³²⁴ The incidence of postthoracotomy respiratory complications has shown an overall decline to less than 10%, whereas the cardiac complication rate has not changed.² Improvements in postoperative care, specifically pain management, are the major cause of this decline.

There are multiple sensory afferents that transmit nociceptive stimuli following thoracotomy (Fig. 53.56). These include the incision (intercostal nerves T4-T6), chest drains (intercostal nerves T7-T8), mediastinal pleura (vagus nerve, CN 10), central diaphragmatic pleura (phrenic nerve, C3-C5),³²⁵ and ipsilateral shoulder (brachial plexus). There is no one analgesic technique that can block all these various pain afferents, so analgesia should be multimodal. The optimal choice for an individual patient depends on patient factors (i.e., contraindications, preferences), surgical factors (i.e., type of incision), and system factors (i.e., available equipment, monitoring, nursing support). The ideal postthoracotomy analgesic technique will include three classes of drugs: opioids, antiinflammatory agents, and local anesthetics.

SYSTEMIC ANALGESIA

Opioids

Systemic opioids alone are effective in controlling background pain, but the acute pain component associated with cough or movement requires plasma levels that produce

sedation and hypoventilation in most patients. Even when administered by patient-controlled devices, pain control is generally poor³²⁶ and patients have interrupted sleep patterns when serum opioid levels fall below the therapeutic range.

Nonsteroidal Antiinflammatory Drugs

NSAIDs can reduce opioid consumption more than 30% following thoracotomy and are particularly useful treating the ipsilateral shoulder pain that is often present postoperatively and is poorly controlled with epidural analgesia. NSAIDs act through reversible inhibition of COX, which has antiinflammatory and analgesic effects but can also be associated with decreased platelet function, gastric erosions, increased bronchial reactivity, and decreased renal function. Acetaminophen is an antipyretic/analgesic with weak COX inhibition and can be administered orally or rectally in doses up to 4 g/day. It is effective against shoulder pain and has a low toxicity compared with more potent COX-inhibiting NSAIDs.³²⁷

Ketamine

Ketamine is used increasingly for postthoracotomy pain as part of multimodal analgesic therapy in combination with regional analgesia, opioids, and antiinflammatory agents.³²⁸ Ketamine can be started intraoperatively as low-dose boluses or infusions and continued postoperatively as an infusion. Common postoperative infusion doses are in the range of 0.1 to 0.15 mg/kg/h.³²⁹ The possibility of psychomimetic effects with ketamine is always a concern but is rarely seen with analgesic, subanesthetic doses. Although perioperative ketamine is useful to reduce acute postthoracotomy pain, it is unclear if it has any benefit in reducing chronic postthoracotomy pain.³³⁰

Dexmedetomidine

Dexmedetomidine, a selective adrenergic alpha-2 receptor agonist, has been reported as a useful adjunct for postthoracotomy analgesia and can significantly decrease the requirement for opioids when used in combination with other analgesics.³³¹ Maintenance infusion doses for analgesia in children and adults are in the range of 0.3 to 0.4 µg/kg/h.³³² It is associated with some hypotension, but it seems to preserve renal function.

Intravenous Lidocaine

Intra- and postoperative lidocaine infusions are frequently included in multimodal analgesic regimens for a wide variety of surgical procedures.³³³ Commonly used doses range between 1 to 2 mg/kg/h. Intravenous lidocaine has not been well studied for postthoracotomy/VATS pain. Small studies of intravenous lidocaine in thoracic surgery have had mixed results.^{334,335}

Gabapentinoids

Gabapentin and pregabalin are well known drugs used to treat chronic pain syndromes. Their usefulness in treating acute pain following thoracic surgery is unclear. A single dose of preoperative gabapentin did not show any benefit when used in conjunction with epidural analgesia.³³⁶ One study of postthoracotomy pain using intravenous morphine analgesia showed a benefit when gabapentin was administered pre- and postoperatively.³³⁷

LOCAL ANESTHETICS/NERVE BLOCKS

Intercostal Nerve Blocks

Regional blocks of the intercostal nerves supplying the dermatomes of the surgical incision can be an effective adjunct to methods of postthoracotomy analgesia. These can be done percutaneously or under direct vision when the chest is open. The duration of analgesia is limited to the duration of action of the local anesthetic used, and the blocks will need to be repeated to have any useful effect on postoperative lung function. Indwelling intercostal catheters are an option but they can be difficult to position reliably percutaneously. Nerve blocks are useful supplements for the pain associated with the multiple small-port incisions and chest drains after VATS. It is important to avoid injection into the intercostal vessels, which are adjacent to the nerve in the intercostal groove. It is also important to place the block near the posterior axillary line to be certain to block the lateral cutaneous branch of the intercostal nerve. Total bupivacaine dose for a single session of blocks should not exceed 1 mg/kg (e.g., for a 75-kg patient: 3 mL bupivacaine 0.5% with epinephrine 1:200,000 at each of 5 levels).

Liposomal encapsulated bupivacaine has a slow release of local anesthetic over a period of 72 to 96 hours. Liposomal bupivacaine was originally introduced for local wound infiltration; however, it has been also used for intercostal blocks for thoracotomy and VATS. In combination with multimodal techniques, the postoperative analgesia may be comparable to thoracic epidural analgesia.³³⁸ The onset of useful analgesia with liposomal bupivacaine is at least 45 minutes, which may be a problem if it is injected only at the end of surgery.³³⁹

Epidural Analgesia

The routine use of neuraxial analgesia for postthoracotomy patients is a well-established concept. Spinal injection of opioids can have a duration of analgesia that approaches 24 hours after thoracotomy. Because of the concerns of possible infection with subarachnoid catheters and the need to repeat spinal injections, investigation and therapy has focused on epidural techniques. A meta-analysis of respiratory complications after various types of surgery has shown that epidural techniques reduce the incidence of respiratory complications.³⁴⁰ Thoracic epidural analgesia for thoracic surgery with infusions of local anesthetic and opioids has become the “gold-standard” against which other techniques of postthoracotomy analgesia are measured. Opioid and local anesthetic combinations provide better analgesia at lower doses than either drug alone.³⁴¹ The use of epidural infusions has an excellent record for patient safety when used on routine postoperative surgical wards.³⁴² The use of a paramedian approach to the epidural space in the midthoracic levels (Fig. 53.57) has improved the success rate for many clinicians. Ultrasound guidance has not yet proven to be as useful for thoracic epidural catheter placement as it has for other types of regional blockade.³⁴³ Identification of the epidural space is most commonly performed with a loss-of-resistance technique that is operator dependent. After injection of a small volume of saline (5 mL) through the Tuohy needle, the epidural pressure can be transduced and a typical waveform can be seen that identifies the epidural space with a high degree of sensitivity and specificity.³⁴⁴

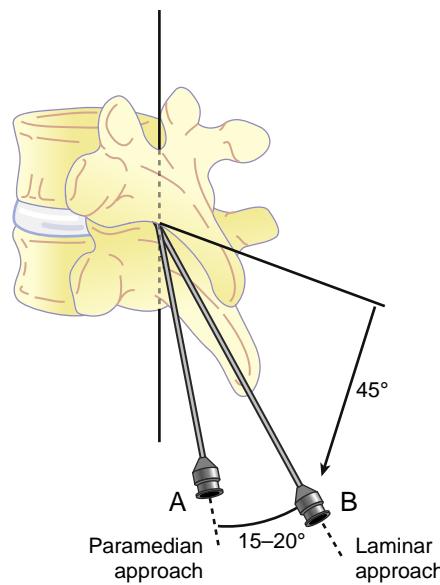


Fig. 53.57 (A) The paramedian approach to the epidural space is now favored by most anesthesiologists at the midthoracic levels. The needle is inserted 1 cm lateral to the superior tip of the spinous process and then advanced perpendicular to all planes to contact the lamina of the vertebral body immediately below. The needle is then “walked” up the lamina at an angle rostrally (45 degrees) and medially (20 degrees) until the rostral edge of the lamina is felt. The needle is then advanced over the edge of the lamina seeking a loss of resistance on entering the epidural space after transversing the ligamentum flavum. (B) The laminar approach is favored by some practitioners. The needle is inserted next to the rostral edge of the spinous process and advanced straight without any angle from the midline. (Reprinted with permission from Ramamurthy S. Thoracic epidural nerve block. In: Waldman SD, Winnie AP, eds. *Interventional Pain Management*. Philadelphia: Saunders; 1996.)

Research has shed light on the pharmacology, which underlies the synergy between local anesthetics and opioids to produce segmental epidural analgesia. In a double-blind randomized study, Hansdottir and associates³⁴⁵ compared epidural infusions of lumbar sufentanil, thoracic sufentanil, and thoracic sufentanil plus bupivacaine (S+B) for postthoracotomy analgesia. Infusions were titrated for equianalgesia at rest. Thoracic sufentanil plus bupivacaine provided significantly better analgesia with movement and less sedation than the other infusions. Although sufentanil dosages and serum levels were significantly lower in the combined (S+B) group than in the other two groups, lumbar cerebral spinal fluid levels of sufentanil at 24 and 48 hours were higher in the combined group than in the thoracic sufentanil group (this suggests that the local anesthetic facilitates entry of the opioid from the epidural space into the cerebral spinal fluid).

In patients with severe emphysema, analgesic doses of thoracic epidural analgesia plus bupivacaine do not cause any significant reduction in lung mechanics or increase in airway resistance.³⁴⁶ In volunteers, a thoracic level of epidural blockade increases FRC.³⁴⁷ This increase is largely because of an increase in thoracic gas volume caused by a fall in the resting level of the diaphragm without a fall in tidal volume. Differences in lipid solubility that create relatively minor clinical differences in the effects of opioids when used systemically cause major differences in the effects of these same opioids when used neurally. The highly lipid-soluble agents (e.g., fentanyl, sufentanil) are

associated with narrow dermatomal spread, rapid onset, and low incidence of pruritus/nausea, and can be potentiated by epinephrine. However, these lipid-soluble agents have significant absorption and systemic effects when used as epidural infusions.³⁴⁸ For incisions that cover many dermatomes (e.g., sternotomy) or for procedures that have combined abdominal and thoracic incisions (e.g., esophagectomy), the hydrophilic opioids (e.g., morphine, hydro-morphone) are preferable.

Paravertebral Block

The paravertebral space is a potential space deep to the endothoracic fascia that the intercostal nerve traverses as it passes from the intervertebral foramen en route to the intercostal space (Fig. 53.58). A catheter can be placed in the thoracic paravertebral space either percutaneously or by approaching the space anteriorly and directly when the chest is open intraoperatively.

There is also a combined percutaneous/direct-vision method in which the tip of the Tuohy needle is advanced percutaneously into the paravertebral space under direct vision either during open thoracotomy or VATS. The tip of the needle is seen to enter the paravertebral space and the pleura is not punctured. Saline is injected via the Tuohy needle to hydrodissect the paravertebral space and an epidural catheter is passed into the pocket that has been created in the paravertebral space and then secured at the skin.

Paravertebral local anesthetics provide a reliable multi-level intercostal blockade that tends to be unilateral with a low tendency to spread to the epidural space. Clinically the analgesia is comparable to that from epidural local anesthetics.³⁴⁹ Studies comparing paravertebral versus thoracic epidural analgesia for thoracotomies have suggested the following advantages for paravertebral blockade³⁵⁰: comparable analgesia; fewer failed blocks; decreased risk of neuraxial hematoma; and less hypotension, nausea, or

urinary retention. Because there is the option to place the paravertebral catheter under direct vision, this may contribute to the lower incidence of failed blocks versus thoracic epidural analgesia.

Paravertebral infusions in combination with NSAIDs and systemic opioids are a reasonable alternative to epidural techniques in children or some patients with contraindications to neuraxial blockade. Using common therapeutic doses (e.g., 0.1 mL/kg/h of bupivacaine 0.5%), serum bupivacaine levels can approach toxic levels by 4 days.³⁵¹ An alternative regime for paravertebral infusions is lidocaine 1% (1 mL/10 kg/h; maximum 7 mL/h). It has not yet been demonstrated if paravertebral analgesia can contribute to a decrease in respiratory morbidity in high-risk cases, which has been shown for thoracic epidural analgesia.³⁵²

Ultrasound-Guided Blocks

The increasing use of ultrasound in regional anesthesia has improved the success of percutaneous paravertebral blocks³⁵³ and has enabled the development of several useful new blocks for postthoracotomy/VATS analgesia.

The serratus anterior plane block is performed at the level of the fifth rib in the midaxillary line. At this level, the serratus anterior muscle can be identified overlying the ribs, with the latissimus dorsi muscle lying superior to the serratus muscle. Needle insertion can be performed in-plane or out-of-plane, depending on provider preference. The serratus anterior plane block can be achieved by injecting local anesthetic either above or below the serratus muscle, with equivalent analgesic spread with both techniques. Serratus anterior plane block has been shown to improve the analgesia provided by patient-controlled morphine.³⁵⁴

The ESP block is an ultrasound-guided block for both acute and chronic postthoracotomy pain. It may, in fact, be a variant of the paravertebral block. Injection of 20 mL of solution into the fascial plane deep into the erector spinae

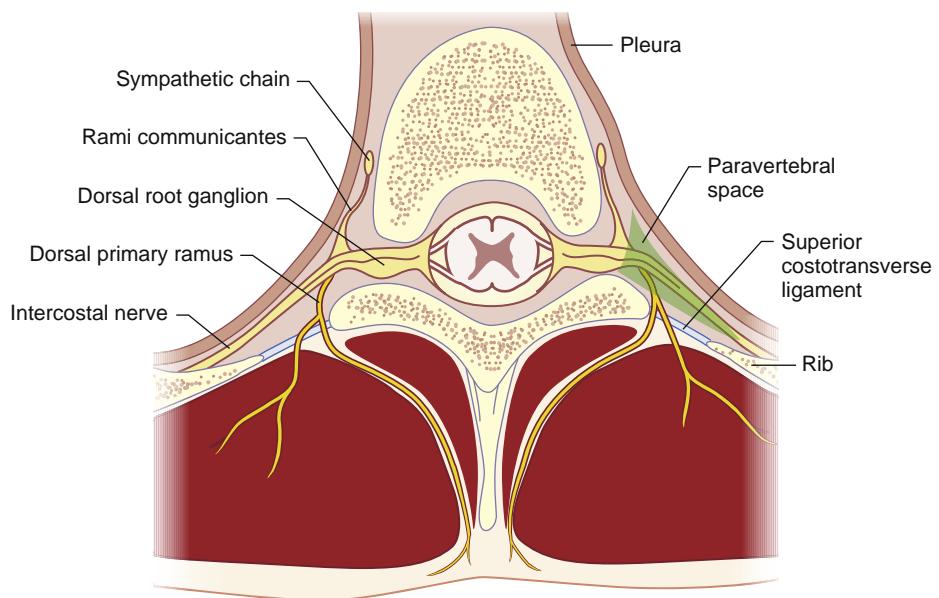


Fig. 53.58 Diagram of the paravertebral space. The space is bound medially by the vertebral body, posteriorly by the costotransverse ligaments and the heads of the ribs, and anteriorly by the endothoracic fascia and parietal pleura. (From Conacher ID, Slinger PD. *Thoracic Anesthesia*. 3rd ed. Kaplan J, Slinger P, eds. Philadelphia: Churchill Livingstone; 2003.)

muscle at the level of the T5 transverse process can result in a spread of injectate from C7 to T8 vertebral levels.³⁵⁵ This block has been described for postthoracotomy analgesia rescue in a case of failed epidural analgesia in a patient receiving prophylactic anticoagulation.³⁵⁶ The benefit of an ESP block over a paravertebral block may be the more obvious end-point for an ESP block as the needle tip contacts the transverse process of the vertebra. An ultrasound-visible regional anesthetic needle (e.g., 8 cm, 17-gauge) is inserted to contact the transverse process of the appropriate thoracic vertebra deep to the anterior fascia of the erector spinae muscle (Fig. 53.59). A total of 20 to 25 mL of local anesthetic solution (e.g., 0.2% ropivacaine) is administered in 5 mL aliquots under direct vision. A catheter is then passed 5 cm distal to the tip of the needle and an infusion of 5 to 8 mL/h is begun.

POSTOPERATIVE PAIN MANAGEMENT

PROBLEMS

Shoulder Pain

Ipsilateral shoulder pain is very common after thoracic surgery. It has been documented in 78% of patients immediately postoperatively.³⁵⁷ In 42% of patients this pain was judged to be clinically relevant. By postoperative day 4, 32% of patients had shoulder pain, but only 7% had clinically relevant shoulder pain. Shoulder pain occurred after both open and VATS surgery; the incidence may be decreased after VATS. This pain was felt to be of two major types:

1. Referred pain (55%). This is thought to originate from phrenic nerve afferent fibers and related to diaphragmatic or mediastinal irritation.
2. Musculoskeletal (45%). This pain was associated with tenderness of the involved shoulder muscles and pain with movement.

Of the two types, the musculoskeletal pain was more intense and more difficult to treat.

Shoulder pain is not treated by any of the common regional blocks performed for thoracic surgery (e.g., thoracic epidural analgesia, paravertebral block). Shoulder pain is most responsive to antiinflammatories. Phrenic nerve infiltration and interscalene brachial plexus block³⁵⁸

have had some success but carry a risk of causing diaphragm dysfunction.

Postthoracotomy Neuralgia and Chronic Incisional Pain

In one prospective study, chronic postoperative pain at 6 months was documented in 33% of patients after thoracotomy and 25% after VATS.³⁵⁹ In this study, chronic pain was not associated with preoperative psychosocial measurements found to correlate with chronic postoperative pain in other types of surgery. Chronic pain was associated with acute postoperative pain. This suggests that chronic pain after thoracic surgery may be partially preventable by intensive management of acute postoperative pain.³⁶⁰

MANAGEMENT OF OPIOID TOLERANT PATIENTS

The opioid tolerant patient requiring thoracic surgery presents a significant challenge. Patients may be using physician prescribed opioids for pain related to their thoracic pathology, or other chronic pain syndromes. Active abusers of narcotics or those in a rehabilitation program receiving daily methadone also are included in this group. Whenever possible, patients should take their regular analgesia or methadone preoperatively; otherwise substitute opioids must be provided. The opioid doses required to produce adequate postoperative analgesia are increased.

A multimodal analgesic regimen is optimal. A choice must be made regarding the method of increased opioid delivery, either systemically and/or through an epidural. An increased narcotic dose may be provided in the epidural solution, or standard narcotic concentrations may be used in the epidural with additional systemic narcotic. de Leon-Casasola and Yarussi³⁶¹ report that higher epidural doses of opioid can curtail the appearance of narcotic withdrawal in most patients. More frequently, the patient receives a standard or slightly increased concentration of opioid in the epidural infusion and additional systemic opioid to minimize the occurrence of withdrawal. A convenient way to provide drug delivery in patients not immediately able to take oral medication is in the form of a transdermal fentanyl patch. Systemic opioids can be provided as a continuous intravenous infusion or in oral format.

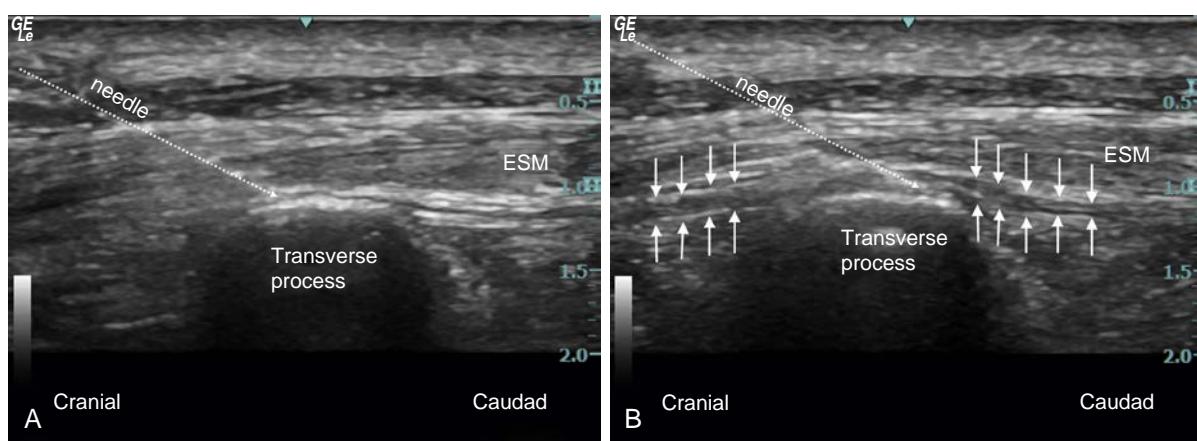


Fig. 53.59 (A) The erector spinae plane block. The ultrasound probe is placed lateral to the spinous process to obtain a parasagittal view of the tip of the targeted transverse process with overlying erector spinae muscle (ESM). The block needle (dotted arrow) is advanced in a cranial-caudal direction to contact the transverse process. (B) Correct needle tip position is signaled by linear spread of local anesthetic (solid arrows) deep to the ESM and superficial to the transverse process. (Photos courtesy KJ Chin Medicine Professional Corporation.)

Patient-controlled analgesic techniques are often difficult to manage in these patients and they may be best managed with fixed dosage regimens that are modified as needed. Ultimately, after dose titration the patient may be receiving both increased epidural opioid and greater than preoperative doses of systemic opioid, without significant side effects. Patients in whom epidural bupivacaine-morphine analgesia is inadequate may respond to a switch to bupivacaine-sufentanil.³⁶² Patients in drug rehabilitation programs with methadone may be reluctant to modify their methadone dose perioperatively, having struggled to establish a stable dose in the past. They frequently can take their full methadone dose throughout the perioperative period.

Supplemental therapies to be considered for these patients include adding epinephrine 5 µg/mL to the epidural infusion solution and the addition of low-dose continuous intravenous ketamine infusions.³⁶³ All opioid-tolerant patients require frequent adjustment of analgesic doses. Despite this, pain scores of 4 to 5 out of 10 with movement are often the lowest achievable. The increased analgesic requirements for opioid-tolerant patients are for a longer duration postoperatively than the usual need for analgesia in opioid-naïve patients.

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MUHAMMAD F. SARWAR, BRUCE E. SEARLES, MARC E. STONE, and LINDA SHORE-LESSERSON

KEY POINTS

- Common cardiac surgical procedures in adults include coronary revascularization with either cardiopulmonary bypass (CPB) or off pump, as well as cardiac valve repair or replacement for valvular regurgitation or stenosis, surgical management of heart failure (e.g., ventricular assist devices, extracorporeal membrane oxygenation, cardiac transplantation), initial repair of or reoperation for congenital heart disease, surgical ablation of atrial fibrillation, pericardiocentesis or pericardectomy, and repair of traumatic injuries to the heart or thoracic aorta.
- Patients undergoing “redo” cardiac surgery (i.e., those who have previously had a median sternotomy) warrant special concern about the possibility of sudden, massive hemorrhage. At least 2 units of blood should be immediately available for all such cases.
- The choice of anesthetic drugs and techniques for inducing anesthesia should include consideration of the patient’s cardiac pathophysiology and other comorbid conditions. Hypotension may result from vasodilation secondary to decreased sympathetic tone induced by anesthetics, particularly in patients with poor left ventricular function. Conversely, hypertension may occur from preinduction anxiety or sympathetic stimulation caused by laryngoscopy and endotracheal intubation.
- During the prebypass period, hemodynamic and metabolic stability of the patient should be achieved while making preparations for CPB. The degree of surgical stimulation varies markedly during this period.
- CPB activates the extrinsic and intrinsic coagulation pathways and alters platelet function through the influence of hemodilution, hypothermia, and contact activation by bypass circuit materials.
- Problems that may occur during the postbypass or postoperative time periods include hypotension resulting from surgical or technical failure, left or right ventricular dysfunction, vasoplegia syndrome, or left ventricular outflow tract obstruction. Other potential problems include dysrhythmias, pulmonary complications (e.g., atelectasis, bronchospasm, mucus or blood plugging of the endotracheal tube, pulmonary edema, hemothorax, pneumothorax), metabolic disturbances (e.g., hypokalemia, hyperkalemia, hypocalcemia, hypomagnesemia, hyperglycemia), and bleeding and coagulopathy.
- The Society of Thoracic Surgeons (STS), the Society of Cardiovascular Anesthesiologists, and the American Society of ExtraCorporeal Technology published a joint statement on practice guidelines for transfusion and blood conservation in cardiac surgery. A European Guideline published by the European Association for Cardio-Thoracic Surgery and European Association of Cardio-thoracic Anesthesiology confirm these recommendations. The guidelines include recommendations regarding the following: (1) use of drugs that decrease postoperative bleeding, including antifibrinolytic drugs; (2) techniques for conserving blood and minimizing hemodilution, including cell saver sequestration, retrograde priming of the pump, and normovolemic hemodilution; and (3) implementation of transfusion algorithms supported with point-of-care testing.
- The incidence of overt postoperative stroke after isolated coronary artery bypass grafting (CABG) surgery has decreased significantly to 1.2% despite the more frequent and current prevalence of diabetes mellitus and hypertension. The major risk factor for central nervous system injury or dysfunction is particulate and microgaseous emboli; other factors include cerebral hypoperfusion and the inflammatory response to surgery and CPB.
- STS guidelines state that blood glucose levels should be maintained at less than 180 mg/dL throughout the perioperative period, although many centers treat cardiac surgical patients somewhat more aggressively with continuous insulin infusions in an attempt to keep glucose levels lower than 150 mg/dL. Hypoglycemia should be avoided.

KEY POINTS—cont'd

- Postoperative pain after median sternotomy or thoracotomy causes enhanced sympathetic tone and may lead to myocardial ischemia secondary to increased heart rate, pulmonary vascular resistance, myocardial work, and myocardial oxygen consumption. Furthermore, pain may cause "splinting" that interferes with the patient's ability to cough and clear secretions and leads to postoperative respiratory insufficiency.
- Common procedures performed in "hybrid" operating rooms or cardiac interventional suites include electrophysiology procedures and procedures that involve percutaneous management of structural heart lesions. These include valvular lesions and atrial or ventricular septal defects. Other percutaneous procedures performed in non-OR locations include placement of ventricular assist devices, extracorporeal membrane oxygenation, and aortic endovascular stenting.

Cardiovascular Disease in the 21st Century

AGE, GENDER, AND RACE

An estimated 82,600,000 U.S. adults (<1 in 3) have one or more types of cardiovascular disease (CVD), of whom approximately half are 60 years old or older.¹ The prevalence of CVD will likely increase because of the "graying" of the United States (i.e., the aging of our population) and the increasing incidences of obesity and hypertension.² Although mortality from coronary artery disease (CAD) specifically has decreased since the 1970s, CVD remains the leading cause of death for both men and women in the United States (Fig. 54.1). Furthermore, approximately 7,588,000 inpatient cardiovascular operations and procedures are performed yearly in the United States, with direct and indirect costs totaling approximately \$315.4 billion.³ As the current healthcare reforms expand treatment coverage, these costs will probably increase.²

Despite the common perception that CVD affects mainly men, this is true only in younger age groups. The sex distribution of CVD changes with age; CVD becomes equally prevalent between the sexes by the age of 60 years, and by the age of 80 years, more women than men are affected.¹ The impact of CVD on the health status of U.S. women has

gained recognition and is the focus of public education efforts such as the "Go Red for Women" campaign sponsored by the American Heart Association (AHA) and the "Red Dress" project sponsored by the Department of Health and Human Services, the National Institutes of Health, and the National Heart, Lung, and Blood Institute.⁴ Furthermore, a series of editorials and articles in the *Journal of Thoracic and Cardiovascular Surgery*⁵ and gender-specific practice guidelines for coronary artery surgery in the *Annals of Thoracic Surgery*⁶ have emphasized sex differences that affect patients who undergo cardiac surgical procedures. For example, using internal mammary artery (IMA) grafts significantly reduces mortality in patients of both sexes, but, until more recently, these grafts were underused in women.⁶ Although some studies have shown that women's short-term survival is worse than men's after coronary artery bypass grafting (CABG) surgery,⁷ others have found that 5-year post-CABG survival is actually better in women than in men.⁸

Mortality resulting from CVD has been consistently more frequent in black than white patients.¹ In 2008, the overall CVD-related death rate per 100,000 persons was 390.4 for black male patients, 287.2 for white male patients, 277.4 for black female patients, and 200.5 for white female patients. Furthermore, racial disparities have been reported in outcomes after CABG: both unadjusted mortality rates and mortality rates adjusted for patient-related characteristics are higher in black patients than in white patients.⁹ In fact, as an unfortunate consequence of the public release of quality information through CABG "report cards" in certain states, institutions and individual surgeons may use "racial profiling" in selecting patients for CABG.¹⁰ For example, in New York State, physicians' avoidance of racial and ethnic minorities, who may be at a higher risk for poor outcomes, may have temporarily widened the disparity in CABG use among white versus black and Hispanic patients.

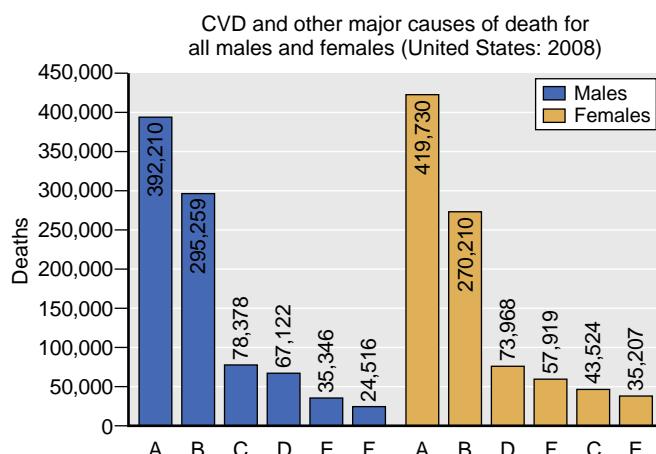


Fig. 54.1 Cardiovascular disease (CVD) and other major causes of death for all male and female members of the U.S. population in 2008. (From Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2–e220; Chart 3–10.)

GENETIC INFLUENCES IN CARDIAC DISEASE

Evolving rapidly beyond racial considerations (which are increasingly losing their medical and scientific meaning in the "melting pot" of the United States), *perioperative genomics* is the study of the unique biologic makeup of surgical patients. This field holds promise for uncovering the biologic reasons that patients with similar risk factors can have dramatically different perioperative clinical outcomes.¹¹ Patients with complex comorbid conditions are

exposed to controlled trauma in the cardiac surgical operating room (Fig. 54.2). The hope is that preoperative risk assessment and outcome prediction will soon include testing for genetic markers related to individual differences in inflammatory, thrombotic, and vascular responses to stress related to cardiopulmonary bypass (CPB) and to the operation itself.

One example is the prevention of perioperative myocardial infarction (MI). Mechanisms in the pathogenesis of myonecrosis include the complex acute inflammatory response to surgery and CPB. Functional genetic variants in cytokine and leukocyte-endothelial interaction pathways are independently associated with the severity of myonecrosis after cardiac surgery.¹² Increased concentrations of the most extensively studied inflammatory marker, C-reactive protein (CRP), are associated with increased mortality in patients who undergo CABG.¹³ Both increased baseline plasma CRP levels and increased acute-phase postoperative plasma CRP levels are genetically determined.¹⁴ Another pathophysiologic process in perioperative MI is coagulation variability with a tendency toward thrombosis. Polymorphisms in platelet activation¹⁵ and thrombin formation have been associated with myocardial injury and with mortality after cardiac surgery.

Genetic factors have been associated with other postoperative complications. Common genetic variants of CRP and interleukin-6 (IL-6) are significantly associated with the risk of stroke¹⁶ and cognitive decline after cardiac surgery.¹⁷ Angiotensin-converting enzyme (ACE) gene polymorphisms predict a patient's risk of respiratory complications that necessitate prolonged mechanical ventilation after cardiac surgery.¹⁸

Research in the field of genetic and molecular determinants of outcomes in patients undergoing cardiac surgery continues. In addition to preoperative risk assessments, intraoperative diagnoses and therefore planning for the postoperative care of the patient will be influenced as new discoveries are made.

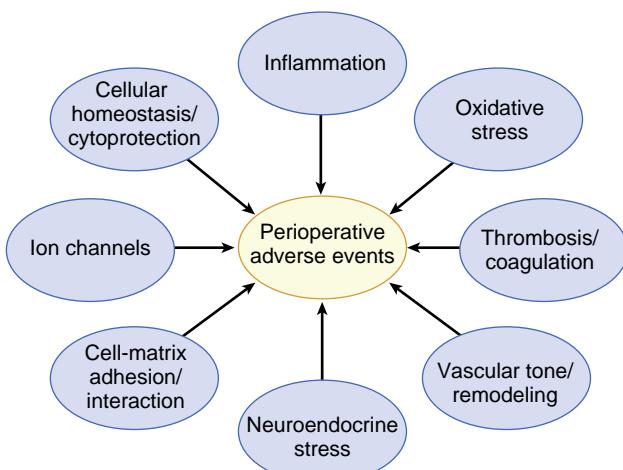


Fig. 54.2 Biologic systems and mechanistic pathways genetically associated with perioperative adverse events. (Redrawn from Podgoreanu MV, Schwinn DA. New paradigms in cardiovascular medicine: emerging technologies and practices: perioperative genomics. *J Am Coll Cardiol*. 2005;46:1965–1977.)

Approach to Anesthesia for the Adult Cardiac Patient

PREOPERATIVE EVALUATION, PREPARATION, AND MONITORING

Heart and Vascular System

Electrocardiography. Standard monitoring of cardiac surgical patients by electrocardiography (ECG) involves using the five-lead electrode system. An electrode is placed on each extremity, and one precordial electrode is placed in the V₅ position (on the left anterior axillary line at the fifth intercostal space). Ischemia detection is greatest (75%) with the V₅ lead. This sensitivity increases to 80% when lead II is paired with a V₅ lead.¹⁹ The addition of a second precordial lead, V₄, increases the sensitivity, thus making it possible to detect nearly 100% of ischemic episodes.²⁰ Currently, most ECG monitors can perform ST-segment analysis automatically with high sensitivity and specificity for detecting ischemia.

Despite appropriate lead selection and the use of automated ST-segment monitoring, perioperative ECG monitoring has important limitations. Visual inspection of the ECG on the monitor has low sensitivity in diagnosing ischemic changes, and automated ST-segment analysis depends on the computer's ability to set the isoelectric and J-point reference points accurately. During cardiac surgical procedures, the set points should be checked before and after bypass, especially persistent changes in heart rate, because the reference points chosen at the beginning of the case may not be accurate under conditions that may arise later.²¹

Arterial and Central Venous Pressure Monitoring

(see also **Chapter 36**). Invasive arterial cannulation and monitoring comprise a standard of care for cardiac surgical patients. Patients' comorbidities often include labile hypertension, atherosclerotic CVD, or both. Furthermore, cardiac surgical technique frequently causes sudden, rapid changes in arterial blood pressure resulting from factors such as direct compression of the heart, impaired venous return caused by retraction and cannulation of the great vessels, and arrhythmias resulting from mechanical stimulation.²² In addition, sudden, significant blood loss may induce hypovolemia and hypotension. Finally, during nonpulsatile CPB, noninvasive blood pressure recordings are not accurate. Intraarterial monitoring provides continuous, real-time, beat-to-beat assessment of arterial perfusion pressure and waveform throughout the cardiac surgical procedure. Having an indwelling arterial catheter also enables the frequent drawing of arterial blood for laboratory analyses.²²

Although the radial artery is the most commonly accessed site, the femoral, brachial, ulnar, dorsalis pedis, posterior tibial, and axillary arteries can also be used. The pressures measured in the peripheral arteries are different from the central aortic pressure because the arterial waveform becomes progressively more distorted as the signal is transmitted down the arterial system.²² Although the mean arterial pressure (MAP) measured in the peripheral arteries is usually similar to the central aortic pressure, this may change after CPB is initiated.²³ When cannulating a radial artery, one should consider the native state of the

collateral circulation in the hand and the possible surgical use of a radial artery free graft as an arterial conduit. If a radial arterial graft is to be harvested, it is usually taken from the nondominant hand or arm; thus, the arterial line should be placed on the dominant side.

Central venous access is also standard of care during cardiac surgery. In addition to monitoring central venous pressure (CVP), central venous access provides a portal for intravascular volume replacement, pharmacologic therapy, and the insertion of other invasive monitors, such as pulmonary artery (PA) catheters. In addition, a CVP catheter can be used to measure the filling pressure of the right ventricle and estimate intravascular volume status.²² Although the CVP does not directly reflect left-sided heart filling pressure, it may be used as an estimate of left-sided pressures in patients with good left ventricular (LV) function. Following trends is more useful than relying on an individual measurement.²² In many patients, using a central venous catheter may offer a better risk-to-benefit ratio than using a PA catheter.²⁴ For the accurate measurement of pressure, the distal end of the catheter must lie within one of the large intrathoracic veins or the right atrium.²²

An internal jugular vein is most commonly selected for catheterization because it provides ease of approach and optimal distance from the operative field. A femoral or subclavian vein can be considered as well, but groin access can be challenging in obese patients and may be inappropriate if femoral bypass cannula placement or vein graft harvesting is necessary. The subclavian approach is also imperfect because it is associated with an increased risk of catheter obstruction during sternal retraction.

The use of ultrasound is being rapidly adopted throughout the United States for facilitating the placement of central venous catheters and reducing the complications associated with them.²⁵ Although ultrasound-guided central catheter placement is easily accomplished and appears to improve patients' outcomes, concerns regarding the associated costs of the required hardware and training are reasons for the lack of universal adoption of this technique (Box 54.1).

Pulmonary Artery Catheterization. The PA catheter is a flow-directed catheter typically placed through an introducer in the central venous compartment via the internal jugular, subclavian, or femoral vein (see also Chapter 36). This catheter can measure PA pressure (PAP), CVP, and pulmonary capillary wedge pressure (PCWP). However, the PCWP can both overestimate and underestimate LV filling pressure (Box 54.2). Some PA catheters are designed with a thermistor to register blood temperature changes, which are used to calculate right-sided heart cardiac output (CO) or ejection fraction (EF) by thermodilution. PA catheters may also have oximetric capabilities to measure mixed venous oxygen saturation (\bar{SvO}_2). Thus, a PA catheter can be used to assess intravascular volume status, measure CO, measure \bar{SvO}_2 , and derive hemodynamic parameters.²²

The CO, the amount of blood delivered to the tissues by the heart, is of particular interest to cardiac anesthesiologists. The product of stroke volume and heart rate, CO is affected by preload, afterload, heart rate, and contractility. PA catheters capable of measuring CO continuously were introduced into clinical practice in the 1990s.²² The correlation of continuous CO measurements with those

BOX 54.1 Some of the Recognized Benefits of and Concerns About Ultrasound-Guided Central Venous Cannulation

Benefits*

- Greater success rate on first attempt
- Fewer overall attempts
- Better access in patients with difficult neck anatomy (e.g., resulting from obesity or prior surgery)
- Fewer complications (e.g., carotid artery puncture, anticoagulant-enhanced bleeding)
- Visible vessel patency, anatomic variants
- Relatively inexpensive technology

Concerns

- Need for personnel to be trained to maintain aseptic technique when using sterile probe sheaths
- Requirement for additional training
- Inability to show surface anatomy
- Potential loss of landmark-guided skills when needed for emergency central venous catheterization

*Ultrasonic guidance of internal jugular vein cannulation can be particularly advantageous in patients with difficult neck anatomy (e.g., short neck, obesity) or prior neck surgery, anticoagulated patients, and infants.

Modified from Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:426.

BOX 54.2 Conditions Resulting in Discrepancies Between Pulmonary Capillary Wedge Pressure and Left Ventricular End-Diastolic Pressure

PCWP > LVEDP

- Positive-pressure ventilation
- PEEP
- Increased intrathoracic pressure
- Non-West lung zone III PAC placement
- Chronic obstructive pulmonary disease
- Increased pulmonary vascular resistance
- Left atrial myxoma
- Mitral valve disease (e.g., stenosis, regurgitation)

PCWP < LVEDP

- Noncompliant left ventricle (e.g., ischemia, hypertrophy)
- Aortic regurgitation (premature closure of the mitral valve)
- LVEDP > 25 mm Hg

LVEDP, Left ventricular end-diastolic pressure; PAC, pulmonary artery catheter; PCWP, pulmonary capillary wedge pressure; PEEP, positive end-expiratory pressure.

Modified from Tuman KJ, Carroll CC, Ivankovich AD. Pitfalls in interpretation of pulmonary artery catheter data. *Cardiothorac Vasc Anesth Update*. 1991;2:1.

measurements obtained by using the intermittent thermodilution method is good in physiologically and thermally stable prebypass and postbypass periods.

Continuous monitoring of \bar{SvO}_2 provides a means to estimate the adequacy of oxygen delivery relative to oxygen consumption.²² Decreases in \bar{SvO}_2 may indicate decreased CO, increased oxygen consumption, decreased arterial oxygen saturation, or decreased hemoglobin concentration. If

it is assumed that oxygen consumption and arterial oxygen content are constant, changes in \bar{SvO}_2 should reflect changes in CO.²² However, London and colleagues found that continuous \bar{SvO}_2 monitoring did not lead to better outcomes than standard PA catheter monitoring.²⁶

Pacing PA catheters are also commercially available. Electrode PA catheters include five electrodes for atrial, ventricular, or atrioventricular (AV) sequential pacing. Paceport PA catheters (Edwards Lifesciences, Irvine, CA) have a port for the insertion of a ventricular wire or of both atrial and ventricular wires for temporary pacing.

The risk-to-benefit ratio involved in using PA catheters has been a subject of controversy since the 1990s. Complications of PA catheter placement include those mentioned in the section on CVP placement, as well as transient arrhythmias, complete heart block, pulmonary infarction, endobronchial hemorrhage, thrombus formation, catheter knotting and entrapment, valvular damage, and thrombocytopenia.²² In addition, a common complication is incorrect interpretation of the data obtained from the PA catheter, with resultant incorrect treatment of the patient.²⁷ Schwann and colleagues published a large, international, prospective observational study showing that using a PA catheter was associated with a more frequent risk of a composite mortality and morbidity outcome than using a CVP alone in patients undergoing CABG surgery.²⁴ Smaller observational trials have also associated the PA catheter with increased morbidity and decreased survival in cardiac surgical patients.^{28,29}

Currently, the trend in the United States is to be selective in deciding which patients may benefit from a PA catheter, especially with the widespread use of transesophageal echocardiography (TEE). Absolute contraindications to PA catheter placement include tricuspid or pulmonic valvular stenosis, right atrial (RA) or right ventricular (RV) masses, and tetralogy of Fallot.²² Relative contraindications include severe arrhythmias and newly inserted pacemaker wires (which may be dislodged by the catheter during insertion). Clearly, patients undergoing low-risk cardiac surgical procedures can be managed safely without PA catheter placement.²² However, many cardiac surgeons and anesthesiologists still use the device in high-risk cardiac operations and in patients with right-sided heart failure (HF) or pulmonary hypertension, particularly to assist in postoperative management (Box 54.3).

Transesophageal Echocardiography. TEE is used in many, if not most, cardiac surgical procedures in the current era. See Chapter 37 for a thorough discussion of this extraordinarily valuable diagnostic and monitoring modality.

Central Nervous System

The incidence of overt postoperative stroke after isolated CABG decreased significantly from 1.6% in the year 2000 to 1.2% in the year 2009, despite the greater prevalence of diabetes mellitus and hypertension in the current era.³⁰ A more subtle entity, postoperative cognitive decline (POCD), or more recently termed delayed neurocognitive recovery as part of the postoperative neurocognitive disorders (PND), has also been described in numerous studies.³¹ However,

BOX 54.3 Possible Clinical Indications for Pulmonary Artery Catheter Monitoring

Major procedures involving large fluid shifts or blood loss in patients with:

Right-sided heart failure, pulmonary hypertension
Severe left-sided heart failure not responsive to therapy
Cardiogenic or septic shock or multiple organ failure
Hemodynamic instability requiring inotropes or intraaortic balloon counterpulsation
Surgery of the aorta requiring suprarenal cross-clamping
Hepatic transplantation
Orthotopic heart transplantation

Modified from Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:435.

BOX 54.4 Mechanisms of and Contributing Factors to Neurologic Lesions

Embolization

Hypoperfusion

Inflammation

Influencing Factors

Aortic atheromatous plaque
Cerebrovascular disease
Altered cerebral autoregulation
Hypotension
Intracardiac debris
Air
Cerebral venous obstruction on bypass
Cardiopulmonary bypass circuit surface
Reinfusion of unprocessed shed blood
Cerebral hyperthermia
Hypoxia

From Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:1070.

the measurement of POCD is complicated by variations in the tests used to assess cognitive function, the timing of these tests, and the diagnostic and statistical definitions of decline.³² Furthermore, studies have shown that compared with nonsurgical and healthy controls, patients who undergo CABG have similar rates of cognitive decline 1 year postoperatively.^{33,34}

Risk factors for central nervous system (CNS) injury or dysfunction after cardiac surgery are listed in Box 54.4.³⁵ The most common cause is thought to be particulate or microgaseous emboli.^{36,37} Other factors include cerebral hypoperfusion, particularly in patients with cerebrovascular disease, and the inflammatory response to surgery and CPB.^{38,39}

Monitoring

TRANSESOPHAGEAL AND EPIAORTIC ECHOCARDIOGRAPHY. TEE allows direct visualization of the first segment of the ascending aorta, the middle distal segment of the aortic arch, and a good portion of the descending thoracic aorta. However, the distal segment of the ascending aorta and the proximal

TABLE 54.1 Grading Aortic Atherosclerosis

Aortic Atheromatous Disease	Echocardiographic Findings
Grade 1	Normal or mild intimal thickening
Grade 2	Severe intimal thickening No protruding atheromas
Grade 3	Atheroma protruding <5 mm into the lumen
Grade 4	Atheroma protruding ≥5 mm into the lumen
Grade 5	Atheroma of any size with a mobile component

Modified from Béique FA, Joffe D, Tousignant G, Konstadt S. Echocardiography-based assessment and management of atherosclerotic disease of the thoracic aorta. *J Cardiothorac Vasc Anesth*. 1998;12:206–220.

midportion of the aortic arch cannot be visualized well because of the interposition of the trachea and bronchi between the TEE probe and these aortic structures. Instead, epiaortic imaging with a handheld, high-frequency probe placed over the ascending aorta or aortic arch can be used to visualize aortic segments that are in the TEE probe's "blind spot."

The echocardiographic finding of atheromatous disease of the aorta has been linked to CNS injury in cardiac surgical patients.⁴⁰ Atherosclerosis of the ascending aorta is present in 20% to 40% of cardiac surgical patients, and the percentage increases with age. The severity of atheromatous disease of the aorta is a strong predictor of death and stroke after CABG (Table 54.1).⁴¹ Using TEE to guide cannula placement or surgical technique significantly reduced the stroke rate in a series of 500 consecutive patients compared with controls in a statewide database.⁴² Avoiding instrumentation of the ascending aorta (the "no touch technique") in patients with severe aortic atherosclerosis has been advocated.⁴³ The addition of epiaortic scanning of the ascending aorta increases the sensitivity of intraoperative echocardiography in identifying significant atheromatous disease in this segment of the aorta. Certainly, this combination of techniques is superior to surgical palpation in detecting such disease.⁴⁴

CEREBRAL OXIMETRY. Cerebral oximetry uses near-infrared spectroscopy technology similar to that used in pulse oximeters. Light-emitting electrodes are placed on the patient's forehead, lateral to the midline, and over both frontal cortices. Because the skull is translucent to infrared light, and because oxygenated and deoxygenated blood have different absorption characteristics when exposed to infrared light of two different wavelengths, regional cerebral oxygen saturation (rSO_2) can be computed from the returning signal. The design of the cerebral oximeter enables it to measure change from the patient's own established baseline and to monitor both frontal lobes simultaneously.

The use of near-infrared spectroscopy has been studied in the perioperative setting; a relative decrease in rSO_2 to less than 80% of the preoperative baseline or to absolute levels less than 50% increased the incidence of adverse postoperative outcomes.^{45,46} These outcomes include POCD,⁴⁷ stroke,⁴⁸ organ dysfunction, mortality,^{49,50} and length of hospital stay.⁵¹ A physiologically derived treatment algorithm for management of perioperative cerebral oxygen

desaturation has been proposed (Fig. 54.3).⁵² As noted by Murkin,³⁵ an important confounder in evaluating the role of monitoring cerebral oximetry is the efficacy of treatment for cerebral desaturation.

A baseline rSO_2 that is low even though the patient is breathing supplemental oxygen (absolute value ≤50%) is an independent risk factor for 30-day and 1-year mortality.⁵³ A baseline rSO_2 could act as a refined marker for preoperative risk stratification and help clinicians identify patients who require more intensive monitoring and care in the postoperative period.^{53,54}

TRANSCRANIAL DOPPLER. Transcranial Doppler (TCD) involves the ultrasonic interrogation of blood flow velocity through the middle cerebral or common carotid arteries as an indirect measure of cerebral blood flow.⁴⁵ The technology has been used extensively as a research tool. For example, in conjunction with cerebral oximetry, TCD has been used to delineate the limits of cerebral autoregulation during CPB.⁵⁵ TCD can also detect cerebral emboli. Contrary to previous information, an association between TCD-detected emboli and POCD is questionable.^{56,57}

A primary limitation of TCD technology has been its inability to discern gaseous from solid emboli.^{45,56} Other general limitations of TCD technology include the following: (1) the quality of information is heavily user dependent; (2) accuracy requires stable and precise probe placement, which can be quite cumbersome; and (3) information is affected by patient-related characteristics, such as skin thickness. These difficulties have limited use of this technology in the perioperative setting.⁴⁵

ELECTROENCEPHALOGRAPHY AND BISPECTRAL INDEX MONITORING. The electroencephalogram (EEG), recorded from multiple adhesive or screw-in scalp electrodes, represents surface cerebral cortical activity (see also Chapters 9 and 10). Awake patients produce a pattern of EEG readings that differs from the pattern produced by patients who are under anesthesia. Establishing a baseline and monitoring the changes from that baseline form the premise of EEG monitoring. Changes in the frequency of EEG signals (slower brain waves) and the reduction of wave amplitude may indicate changes in cortical neuronal function that warrant concern.

Multichannel EEG monitoring is not routinely used in cardiac surgery. However, a resurgence of interest in single- or dual-channel processed EEG monitoring, such as the bispectral index (BIS), has occurred.^{45,58,59} The BIS has been studied as a means to monitor for intraoperative awareness, to reduce overall anesthetic consumption, and to provide information on cerebral perfusion. However, controversy surrounds the usefulness of BIS monitoring in reducing intraoperative awareness.^{45,60–62} Similarly, the effectiveness of BIS monitoring in either guiding the safe reduction of anesthetic dosing or contributing to the success of fast tracking has not been demonstrated by randomized clinical trials in cardiac surgical patients.⁵⁸

With respect to cerebral ischemia, sudden EEG changes during cardiac surgery and CPB can be attributable to correctable problems such as superior vena cava (SVC) obstruction or severe decrease in CO.⁵⁸ The latest iteration of the BIS monitor incorporates bilateral frontal EEG channels, which may increase its ability to detect unilateral

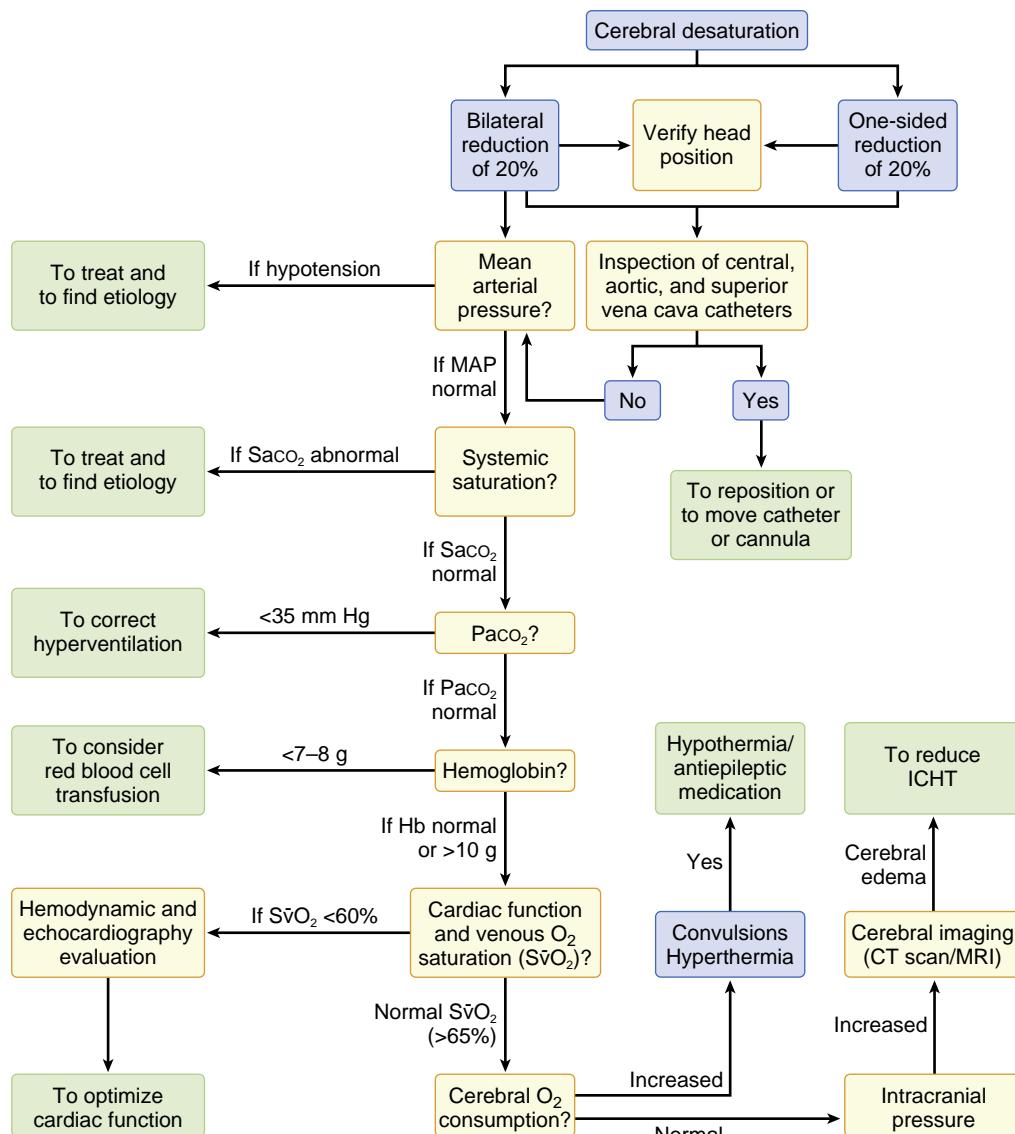


Fig. 54.3 Algorithm for the use of brain oximetry. *CT*, Computed tomography; *ICHT*, intracranial hypertension; *MAP*, mean arterial pressure; *MRI*, magnetic resonance imaging; O_2 , oxygen; $Paco_2$, partial pressure of arterial carbon dioxide; Sao_2 , arterial oxygen saturation; $SV\bar{O}_2$, mixed venous oxygen saturation. (Redrawn from Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy. *Semin Cardiothorac Vasc Anesth*. 2007;11:274–281.)

frontal ischemia, especially if anesthesia is stable, if the insult is sudden, extended, or located in the frontal area, and if the preoperative EEG was normal.^{58,63} However, many variables may confuse EEG interpretation during cardiac surgery. These include hypothermia, the pharmacologic suppression of EEG signals, and interference produced by pump mechanics. In addition, the EEG measures only cortical activity, so ischemic or embolic injury that occurs below the level of the cortex may go undetected. Therefore, the EEG and derived indices are neither sensitive nor specific in detecting cerebral ischemia.⁵⁸

SUMMARY. Currently, evidence-based recommendations cannot be made regarding the efficacy of treatment for abnormal values. Although not yet recognized as a clinical standard of care, neuromonitoring will likely continue to be the subject of significant research effort.

Renal System

Acute kidney injury (AKI) after cardiac surgery remains a significant cause of postoperative morbidity, increased cost of care, later development of chronic kidney disease, and short-term as well as long-term mortality.⁵⁹ Although the pathogenesis of AKI is multifactorial, control of some specific factors may limit its incidence in cardiac surgical patients. Bellomo and associates identified six major injury pathways of cardiac surgery-associated AKI: toxins (both exogenous and endogenous), metabolic factors, ischemia-reperfusion injury, neurohormonal activation, inflammation, and oxidative stress.⁶⁰

Randomized trials of specific potential preventive measures for AKI after cardiac surgery are few. Certainly, all potentially nephrotoxic drugs should be avoided in the perioperative period (Box 54.5).^{59,61} Hydration is, of course, a universally accepted component of strategies to prevent

BOX 54.5 Drugs That Contribute to Kidney Injury

- Radiocontrast agents
- Aminoglycosides
- Amphotericin
- Nonsteroidal antiinflammatory drugs
- β-Lactam antibiotics (specifically contribute to interstitial nephropathy)
- Sulfonamides
- Acyclovir
- Methotrexate
- Cisplatin
- Cyclosporine
- Tacrolimus
- Angiotensin-converting enzyme inhibitors
- Angiotensin receptor blockers

Modified from Bellomo R, Kellum JA, Ronco C. Acute kidney injury. *Lancet*. 2012;380:756–766.

contrast nephropathy.⁶¹ Unfortunately, no pharmacologic strategy has definitive efficacy in preventing early AKI.⁶¹ Atherosclerosis of the ascending aorta appears to be an independent risk factor for AKI.⁶⁰

Intraoperative TEE should be used to identify patients at increased risk for thromboembolic phenomena.^{60,61} Although observational studies have suggested a possible benefit of off-pump procedures and avoidance of aortic manipulation, definitive evidence is lacking.^{60,61} For cardiac surgical cases that require CPB, the duration of aortic cross-clamping should be limited if possible, especially in patients who are at a higher-than-normal risk for renal complications, such as patients with preexisting renal insufficiency.⁶⁰ Hemodynamic instability should be addressed quickly, and intravascular volume should be maintained or rapidly restored.^{60,61} Finally, perioperative hyperglycemia should be avoided.^{60,61}

Clearly, definition of measures that may prevent AKI after cardiac surgery is needed.^{60,61} The cost of this complication to the patient and to society is probably higher than previously thought.⁵⁹

Endocrine System

Glucose Control. Hyperglycemia in surgical patients is a consequence of the inflammatory or stress response to the trauma of surgery. Components of this response include an endocrine response (i.e., increased production of counterregulatory hormones such as cortisol, growth hormone, glucagon, and catecholamines) (Fig. 54.4), an immune response resulting in increased cytokine production, an autonomic response resulting in increased sympathetic stimulation, and altered insulin signaling. These changes increase glucose production, decrease glucose elimination during CPB, and induce insulin resistance, thereby causing hyperglycemia.⁶²

All patients are at risk for developing hyperglycemia during cardiac surgery. Older patients, diabetic patients, and patients with CAD are particularly prone to perioperative hyperglycemia. Although cardiac surgery without CPB initiates a stress response, CPB increases this response many-fold.⁶³ The degree of hyperglycemia depends on several variables associated with the use of CPB, such as the pump

prime fluid selected and the degree of hypothermia induced. Epinephrine and other inotropic drugs may contribute to hyperglycemia after CPB by stimulating hepatic glycogenolysis and gluconeogenesis.

Impaired fasting glucose blood levels before cardiac surgery and persistently increased glucose levels during and immediately after surgical procedures are predictive of longer hospital stay and increased perioperative morbidity and mortality in both diabetic and nondiabetic patients.^{64,65} However, in diabetic patients undergoing cardiac operations, hyperglycemia may only partly explain the increased risk for adverse outcomes.⁶⁵ Immunologic abnormalities common to diabetic patients, such as decreased chemotaxis, phagocytosis, opsonization, bacterial killing, and antioxidant defense, also promote adverse outcomes by increasing diabetic patients' risk of infection.⁶⁶

Glucose blood levels should be controlled, beginning in the preoperative period and continuing until discharge.⁶⁷ However, in a classic study, patients were randomly assigned to intensive intraoperative insulin treatment (to maintain glucose levels at 80–100 mg/dL) or to standard insulin treatment (to keep glucose levels <200 mg/dL).⁶⁸ Surprisingly, the investigators reported a statistically non-significant increase in the incidence of death and stroke in the group receiving intensive insulin treatment. Current Society of Thoracic Surgeons (STS) guidelines state that blood glucose levels should be kept lower than 180 mg/dL throughout the perioperative period.⁶⁹ Some cardiac surgical centers more aggressively administer continuous insulin infusions in an attempt to keep glucose levels lower than 150 mg/dL.

Thyroid Hormone. Fig. 54.5 shows the effect of thyroid hormone on cardiovascular hemodynamics.⁷⁰ Abnormal thyroid function ultimately affects cardiac function in many ways (Table 54.2). During cardiac surgery, the effect of CPB on thyroid hormone production is uncertain. Both increased and decreased levels of thyroid hormone can occur during or immediately after CPB. Free triiodothyronine (T₃), the biologically active form of the thyroid hormone, is frequently reduced in cardiac patients because of the reduced activity of the 5'-monodeiodinase responsible for converting thyroxine (T₄) into T₃ in peripheral tissues.⁷¹ Patients with low T₃ values are predisposed to low CO and therefore death as a complication of cardiac surgery. Patients should be profiled for T₃ levels and labelled high risk if the levels are low preoperatively.⁷²

Notably, hypothyroidism is more common in female than in male patients undergoing CABG.⁷³ Zindrou and associates noted a 17% higher mortality rate in women who underwent CABG while receiving thyroxine replacement therapy for hypothyroidism.⁷⁴ A review of the literature by Edwards and colleagues concluded that ensuring a perioperative euthyroid state in women with hypothyroidism who were undergoing CABG could be helpful in reducing the perioperative mortality of these patients.⁷⁵

Hematologic System

Bleeding is the primary complication of cardiac operations that require CPB. In fact, 10% to 15% of blood product use in the United States is associated with cardiac surgery, and this percentage is increasing, largely because of

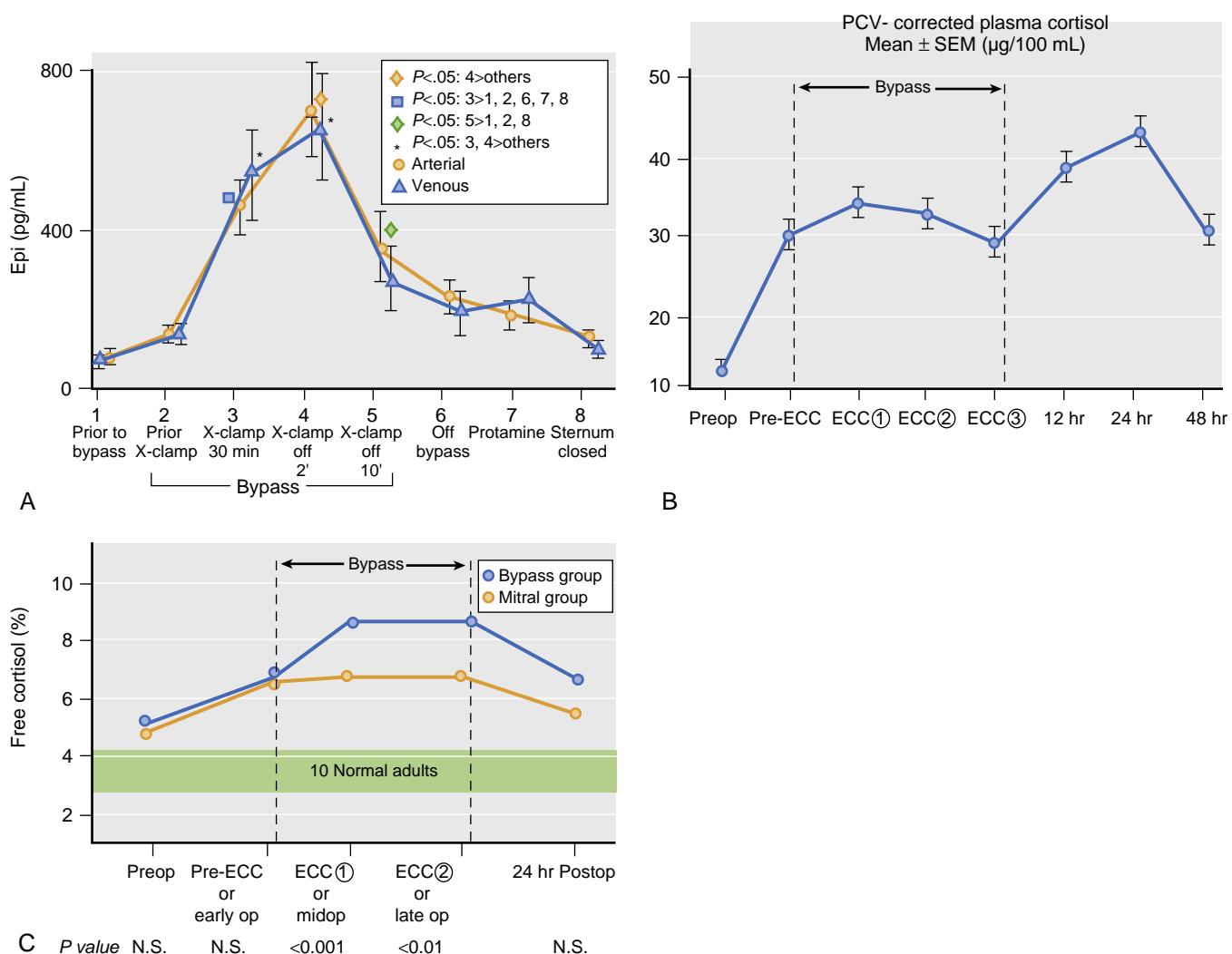


Fig. 54.4 (A) Plasma levels of epinephrine (Epi) during cardiac surgery. Bars indicate standard error of the mean. X-clamp, Cross-clamp. (B and C) Levels of cortisol during cardiac surgery. ECC, Extracorporeal circulation; Midop, intraoperatively; N.S., not significant; op, operatively; PCV, packed cell volume; Postop, postoperatively; Preop, preoperatively. ([A] Redrawn from Reves JG, Karp RB, Buttner EE, et al. Neuronal and adrenomedullary catecholamine release in response to cardiopulmonary bypass in man. *Circulation*. 1982;66:49–55; [B and C] From Taylor KM, Jones JV, Walker MS, et al. The cortisol response during heart-lung bypass. *Circulation*. 1976;54:20–25.)

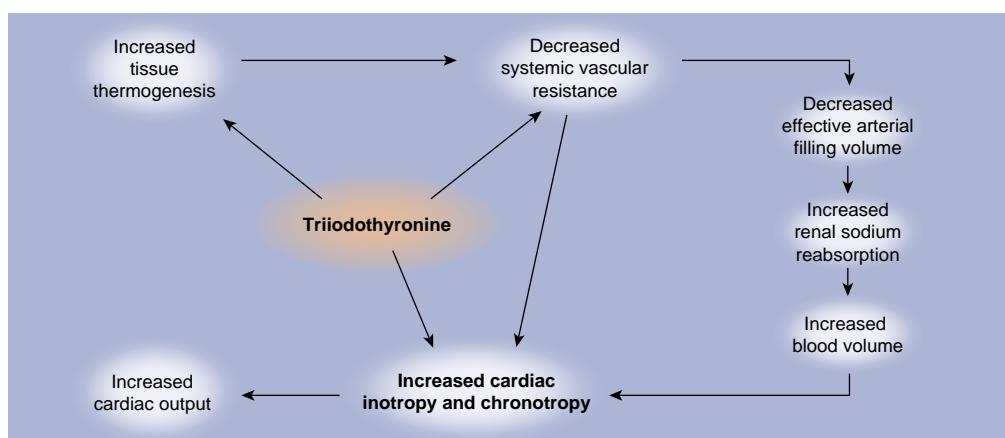


Fig. 54.5 Effects of thyroid hormone on cardiovascular hemodynamics. The diagram shows the way in which triiodothyronine increases cardiac output by affecting tissue oxygen consumption (thermogenesis), vascular resistance, blood volume, cardiac contractility, and heart rate. (Redrawn from Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med*. 2001;344:7.)

TABLE 54.2 Effects of Thyroid Dysfunction on Hemodynamics and Cardiac Function

Parameter	Normal Values	Hyperthyroidism	Hypothyroidism
Blood volume (% of normal value)	100	105.5	84.5
Heart rate (beats/min)	72-84	88-130	60-80
Cardiac output (L/min)	4.0-6.0	>7.0	<4.5
Systemic vascular resistance (dynes·cm ⁻⁵)	1500-1700	700-1200	2100-2700
Left ventricular ejection fraction (%)	>50	>65	≤60
Isovolumic relaxation time (ms)	60-80	25-40	>80

Reprinted with permission from Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med*. 2001;344:501-509. Copyright © 2001 Massachusetts Medical Society.

the increasing complexity of cardiac surgical procedures. Real-world data obtained from a large sample of patients and entered into the STS Adult Cardiac Surgery Database suggest that 50% of patients who undergo cardiac surgical procedures receive a blood transfusion.⁷⁶ Complex cardiac operations such as “redo” procedures, aortic operations, and the implantation of ventricular assist devices (VADs) require blood transfusion much more often than do simpler operations. Donor blood is viewed as a scarce resource that is associated with increased healthcare costs and significant risk to patients. Furthermore, perioperative blood transfusion is associated with worse short-term and long-term outcomes.^{77,78} Hence, reducing bleeding and blood transfusions has become a major focus of quality improvement efforts in cardiac surgery.

Heparin as an Anticoagulant. Since its discovery by Jay McLean, MD, in 1915, heparin has stood the test of time and remains the primary anticoagulant used in cardiac operations that require CPB. The mechanism underlying heparin’s anticoagulant effect centers on the heparin molecule’s ability to bind simultaneously to antithrombin III and thrombin. Modern nomenclature refers to antithrombin III as antithrombin (AT). The binding process is mediated by a unique pentasaccharide sequence that binds to AT. The proximity of AT and thrombin, mediated by the heparin molecule, allows AT to inhibit the procoagulant effect of thrombin by binding to the active-site serine residue of the thrombin molecule.⁷⁹ The inhibitory effect of AT is increased 1000-fold in the presence of heparin. The heparin-AT complex can affect several coagulation factors, but factor Xa and thrombin are the most sensitive to inhibition by heparin, and thrombin is 10 times more sensitive to the inhibitory effects of unfractionated heparin than is factor Xa.⁸⁰

Only approximately one-third of the heparin molecules in a dose of heparin contain the critical pentasaccharide segment that is needed for high-affinity binding to AT. Thus, relatively large doses are required to produce the anticoagulant effect necessary for CPB. In fact, dosing of heparin for CPB is somewhat empiric. After a baseline activated clotting time (ACT) is measured (the normal range is 80-120 seconds), a dose of 300 to 400 units/kg of heparin is given as an intravenous bolus. Commercially available assays are used for calculating the patient’s dose-responsiveness to heparin in vitro. Some practitioners administer heparin at the dose that is indicated by such an in vitro dose-response assay. Subsequent heparin dosing for extracorporeal circulation (ECC) is targeted at maintaining ACT values longer than 400 to 480 seconds. Also available is a heparin concentration monitor that uses protamine titration analysis for ex vivo calculation of the whole blood heparin concentration. This result is often used as an adjunct to the ACT value in confirming an adequate heparin concentration for CPB. Unfortunately, ACT test results vary substantially with clinical conditions and the particular platform used for measurement. Thus, the evidence supporting the use of a threshold of 400 or 480 seconds is almost entirely anecdotal.⁸¹

The dose of heparin used in patients on CPB is based on early landmark work published by Bull and coauthors in 1975.⁸² A small study that sought evidence of thrombin activity during CPB in nonhuman primates and pediatric patients found results supporting a safe lower limit for ACT of 400 seconds.⁸³ In 1979, Doty and colleagues proposed a simplified dosing regimen guided by ACT values without dose-response curves.⁸⁴ The data and recommendations from these few studies constitute the primary basis for current heparin dosing protocols.

Despite heparin’s historic and continued role in anticoagulation for patients maintained on CPB, it is not a perfect anticoagulant. Intrinsic and extrinsic pathway coagulation occurs despite heparin administration, and platelets can still be activated by contact with bypass circuitry and by heparin directly.⁸⁵ Alternative anticoagulants are discussed briefly in the section on heparin-induced thrombocytopenia (HIT).

Monitoring of Anticoagulation. Using ACT to monitor the effectiveness of heparin is not an exact science. Tremendous variability is observed in patients’ anticoagulation responses to a given dose of heparin; reasons for this variability include variations in levels of heparin-binding proteins and AT. Hence, ACT values correlate poorly with actual heparin concentrations. Nevertheless, since the publication of Bull and colleagues’ early work,⁸² ACT has been the mainstay of anticoagulation monitoring in cardiac operations that require CPB.

Many different ACT measurement devices are commercially available, and each uses a different platform for clot detection and endpoint signaling. However, they all involve the addition of whole blood to a tube or channel containing a contact-phase activator. The activator can be celite, kaolin, glass, or any combination thereof. The sample is warmed to 37°C before the measurement technique is performed. Clot formation occurs, and the measurement ends when a change in velocity, pressure, oscillation, electromagnetic

TABLE 54.3 Clinical Variables That Can Affect the Activated Clotting Time

Hemodilution	Prolongs ACT in heparinized patients
Hypothermia	Prolongs ACT
Thrombocytopenia	Prolongs ACT
Platelet inhibitors	Prolongs ACT
Platelet lysis	Shortens ACT
Aprotinin	Prolongs only celite ACT
Surgical stress	Shortens ACT

ACT, Activated clotting time.

forces, or even color is observed, depending on the particular platform of measurement.⁸⁵

Several clinical variables can affect the ACT (Table 54.3). In addition to physiologic variations, the design of ACT measurement devices (which varies across their many manufacturers) also affects ACT normal and therapeutic values. ACTs also correlate poorly with whole blood and plasma heparin levels, and responses to heparin differ somewhat between adult and pediatric patients.⁸⁶ Some authors argue that, because of its poor correlation with heparin concentration, ACT alone is not an adequate monitor of heparin efficacy, and that simultaneous or adjunct monitoring of heparin concentration should also be used during CPB. Prolongation of ACT by non-heparin-related clinical factors, such as hypothermia, hemodilution, or quantitative or qualitative platelet abnormalities, is a well-documented phenomenon, and the anesthesiologist must understand these factors to determine whether it is safe to reduce the heparin dose when the ACT is prolonged. The poor correlation between ACT and measured heparin concentration also makes it possible that a dose reduction will render the heparin concentration inadequate, even when the ACT remains within an acceptable range.

Some point-of-care (POC) monitors, such as the Hepcon HMS system (Medtronic Perfusion Systems, Minneapolis, MN), use a protamine titration assay to calculate the heparin concentration. Despotis et al. suggest that monitoring and maintaining heparin concentration—and thus giving larger doses of heparin—actually protect the hemostatic system and may decrease transfusion requirements.⁸⁷ However, other investigators have not been able to confirm that higher doses of heparin confer better hemostatic protection; markers of ongoing coagulation are essentially the same whether traditional ACT monitoring or heparin concentration monitoring is used.⁸⁸ The 2018 STS, Society of Cardiovascular Anesthesiologists (SCA), and the American Society of ExtraCorporeal Technology (AmSECT) Guidelines state: “Use of heparin concentration monitoring in addition to ACT might be considered, for the maintenance of CPB, as this strategy has been associated with a significant reduction in thrombin generation, fibrinolysis, and neutrophil activation. However, its effects on postoperative bleeding and blood transfusion are inconsistent (class IIb, Level of Evidence B).”⁸¹ An additional recommendation includes: “During CPB, routine administration of heparin at fixed intervals, with ACT monitoring, might be considered

and offers a safe alternative to heparin concentration monitoring. (class IIb, Level of Evidence C).”⁸¹

The high-dose thrombin time (HiTT) is a modification of the thrombin time that is designed to measure the high levels of heparin that are used during CPB.⁸¹ Unlike ACT, the HiTT correlates well with heparin concentration, both before and during CPB, and it is not affected by hemodilution and hypothermia. As a measure of thrombin inhibition, the HiTT is a more specific test of heparin’s effect on thrombin than ACT, and it appears to possess less artificial variability. Preoperative heparin infusions do not affect HiTT values.⁸⁹

Protamine and Reversal of Anticoagulation. Protamine, which has been in clinical use for as long as heparin has, remains the heparin reversal drug of choice in cardiac surgery. The protamine dose required to reverse heparin is somewhat controversial. In the first published study to examine this question, Bull and associates chose a dose of 1.3 mg protamine for every 100 units of heparin to provide a slight excess of protamine from a projected needed amount of 1.2 mg for every 100 units of heparin.⁹⁰ Protamine is usually administered according to the total amount of heparin given (i.e., 1-1.3 mg protamine per 100 units of heparin). This method may result in luxuriant protamine doses, which reduce any theoretic or real risks of heparin rebound but may put the patient at higher risk for bleeding events because of the anticoagulant effect of protamine. Guidelines for the practice of anticoagulation in CPB recommend the following:

1. “It is reasonable to limit the ratio of protamine/heparin to less than 2.6 mg protamine/100 Units of heparin, since total doses above this ratio inhibit platelet function, prolong ACT, and increase the risk of bleeding (class IIa, Level of Evidence C).”⁸¹
2. Because of the risk of heparin rebound in patients requiring high doses of heparin and with prolonged CPB times, low-dose protamine infusion (25 mg/h) for up to 6 hours after the end of CPB may be considered as part of a multimodality blood conservation program (class IIb, Level of Evidence C).⁸¹

Protamine can also be administered at a dose calculated from the heparin concentration, which is measured by a protamine titration assay. Guidelines⁸¹ do support this practice stating that “it can be beneficial to calculate the protamine reversal dose based upon a titration to existing heparin in the blood, since this technique has been associated with reduced bleeding⁸⁷ and blood transfusion” (class IIa, Level of Evidence B).⁸⁷ If the heparin concentration is not measured, the protamine dose can be graphically derived by plotting ACT values throughout the case and creating heparin dose-response curves. The amount of protamine used in this method is based on the circulating concentration of heparin in the patient at the time of reversal. Because, theoretically, no excess protamine exists, these patients may be at risk for heparin rebound and therefore may require additional protamine. In a small study conducted in patients undergoing valve surgery, administering protamine in two divided doses by titration resulted in a larger dose but reduced bleeding, presumably by treating heparin rebound.⁹¹

Unique Hematologic Considerations in Cardiac Surgery

HEMATOLOGIC EFFECTS OF CARDIOPULMONARY BYPASS. The hematologic effects of CPB are complex. Exposure of blood to the surfaces of the extracorporeal circuit is a profound stimulus for inflammatory system upregulation, and activation of the hemostatic system is a component of the normal inflammatory response. According to traditional models of hemostasis, ECC activates both the intrinsic and extrinsic coagulation pathways and directly impairs platelet function. Intrinsic pathway activation can occur by contact activation and the conversion of factor XII to factor XIIa on the various surfaces of the CPB circuit. The tissue factor generated from the wound and the circulating tissue thromboplastin combine to cause the extrinsic activation of coagulation by cell-mediated hemostasis, which involves tissue factor-bearing leukocytes and activated endothelial cells. Tissue factor pathway generation of thrombin has a primary role in CPB-associated hemostasis abnormalities (Fig. 54.6).⁹²

In addition to activating both extrinsic and intrinsic coagulation pathways, CPB directly impairs platelet function through a variety of mechanisms. Platelets express on their surface numerous glycoproteins that serve as receptors for several circulating ligands, such as fibrinogen,

thrombin, and collagen (Fig. 54.7). The components of the bypass circuit adsorb circulating proteins that can serve as foci for platelet attraction and adherence. These surface-bound platelets activate and release the contents of their cytoplasmic granules, which can then serve as localized sources of thrombin generation, or they may embolize to initiate microvascular thrombosis.

Fibrinolytic activity is also increased by CPB. Contact activation leads to the activation of factor XII, prekallikrein, and high-molecular-weight kininogen, which causes endothelial cells to produce tissue plasmin activator, and lysis of fibrin and fibrinogen ensues (Fig. 54.8).

The vascular endothelium is itself an active substrate that is sensitive to circulating mediators, and it expresses and releases anticoagulant and procoagulant factors. When exposed to hypoxia or inflammatory mediators during CPB, the endothelium responds and can induce a relatively prothrombotic state marked by tissue factor upregulation, accelerated platelet adhesion, and increased expression of leukocyte adhesion molecules (Fig. 54.9).⁹³

HEPARIN RESISTANCE, ALTERED HEPARIN RESPONSIVENESS, AND ANTITHROMBIN. Heparin resistance is marked by the inability to raise the ACT to therapeutic levels after administration of the recommended doses of unfractionated heparin. Some investigators have defined heparin resistance as

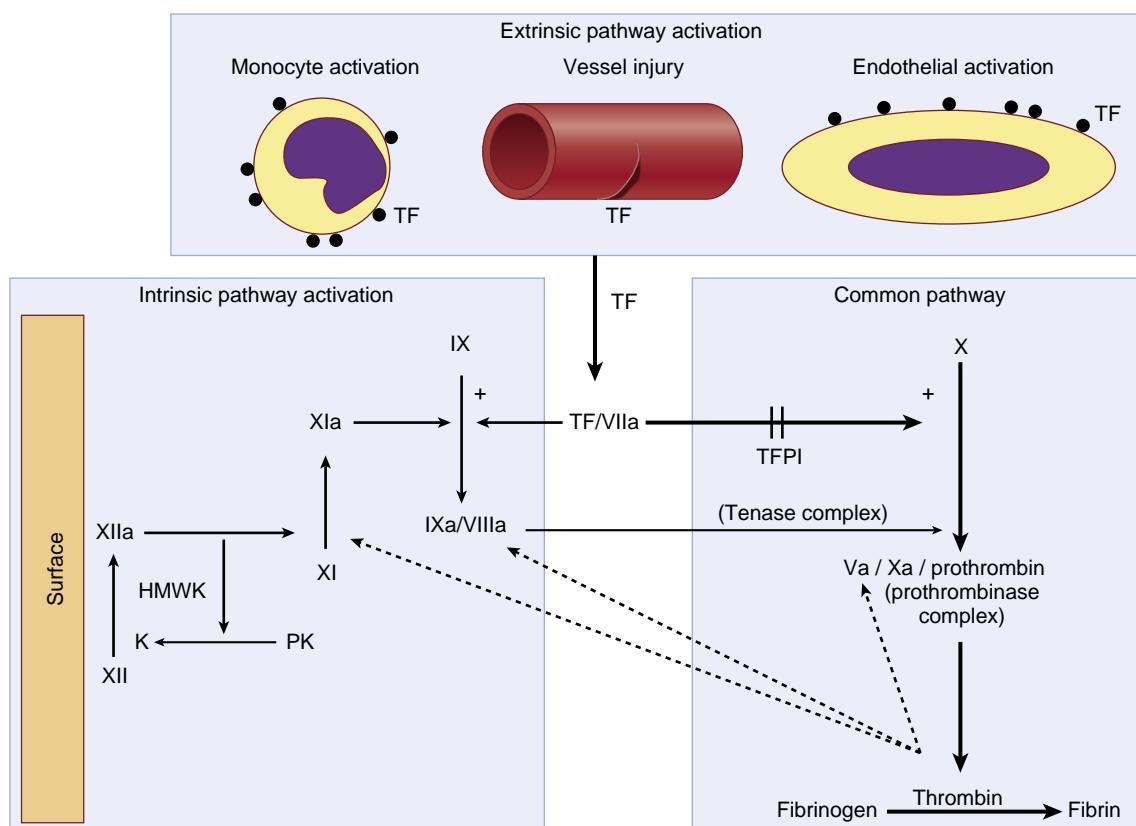


Fig. 54.6 Coagulation can be activated during cardiopulmonary bypass (CPB) by the intrinsic pathway, with surface adsorption and activation of factor XII, high-molecular-weight kininogen (HMWK), and prekallikrein (PK). Activation of the extrinsic pathway during CPB occurs with tissue injury, as well as with systemic inflammation, and it leads to monocyte and endothelial expression of tissue factor (TF). TF, in combination with factor VIIa, starts the common pathway with the activation of factor X to factor Xa. Assembly of the prothrombinase complex on phospholipid surfaces leads to the production of thrombin and conversion of fibrinogen to fibrin. Tissue factor pathway inhibitor (TFPI) inhibits TF/VIIa. Thrombin can overcome this TFPI blockade by activating factors XI, VIII, and V and initiating activation of factor X by the tenase complex. K, Kallikrein. (From Kottke-Marchant K, Sapatnekar S. Hemostatic abnormalities in cardiopulmonary bypass: pathophysiologic and transfusion considerations. *Semin Cardiothorac Vasc Anesth*. 2001;5:187–206.)

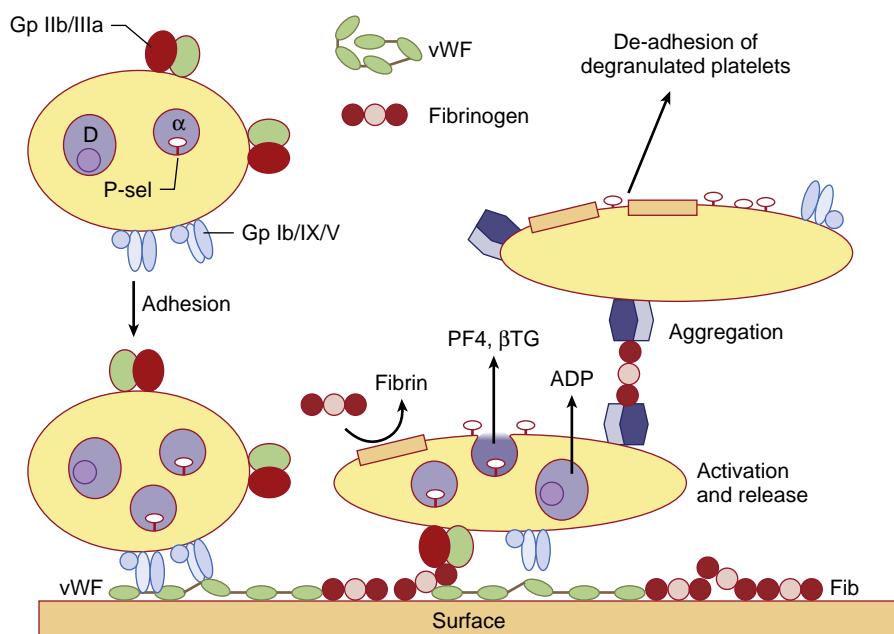


Fig. 54.7 Platelet activation by cardiopulmonary bypass materials is facilitated by rapid adhesion and conformational alteration of plasma proteins, including von Willebrand factor (*vWF*) and fibrinogen (*Fib*). Platelets adhere to *vWF* through the glycoprotein (*Gp*) Ib/IX/X surface glycoprotein and to fibrinogen through the *Gp* IIb/IIIa receptor. Platelet adhesion stimulates intracellular signaling, which leads to degranulation of α granules (platelet factor 4 [*PF4*] and β -thromboglobulin [*β TG*]) and phospholipid reorganization with the formation of coagulation complexes and fibrin formation. Release of adenosine diphosphate (*ADP*) from dense granules and activation of the *Gp* IIb/IIIa receptor also occur and lead to the aggregation of platelets to the adherent layer. Because of shear forces, adherent and aggregated platelets can detach from the membrane and circulate in a degranulated state or form small microaggregates that lodge in the distal vasculature. (From Kottke-Marchant K, Sapatnekar S. Hemostatic abnormalities in cardiopulmonary bypass: pathophysiologic and transfusion considerations. *Semin Cardiothorac Vasc Anesth*. 2001;5:187–206.)

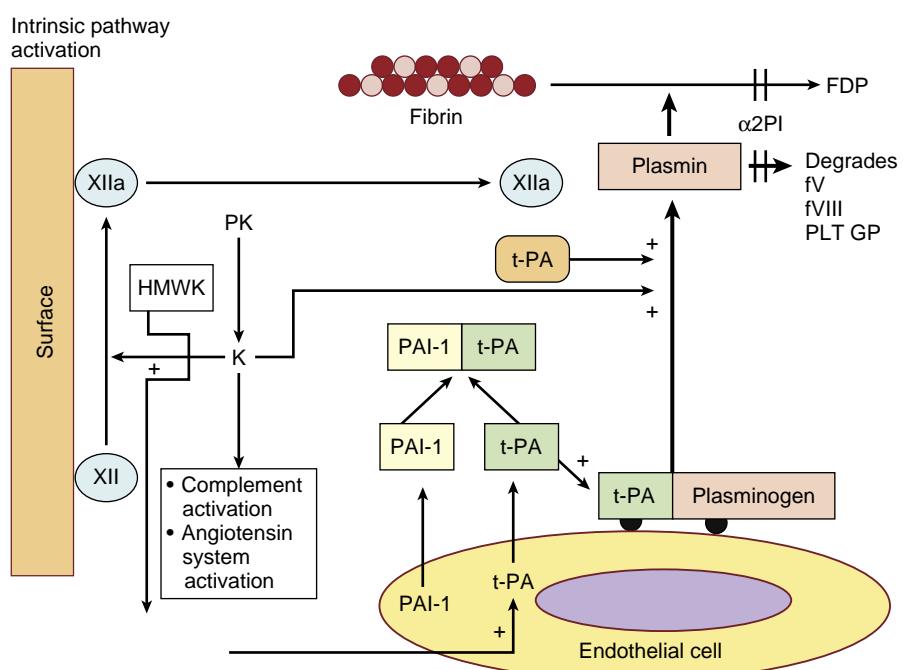


Fig. 54.8 The fibrinolytic system results in the degradation of fibrin by plasmin. The intrinsic factors participate in the fibrinolytic system. Adsorption and activation of factor XII, high-molecular-weight kininogen (HMWK), and prekallikrein (PK) occur on the cardiopulmonary bypass material surfaces. Kallikrein (*K*) and factor XIIa participate in the conversion of plasminogen to plasmin. Plasminogen is also activated by tissue plasminogen activator (t-PA), which is released from endothelial cells, along with its inhibitor, plasminogen activator inhibitor-1 (PAI-1). Plasmin degrades not only fibrin but also coagulation factors V and VIII (fV and fVIII) and platelet surface glycoproteins (PLT GP). Kallikrein plays additional roles in the activation of complement and the angiotensin system, and HMWK accelerates fibrinolysis by stimulating endothelial production of t-PA. FDP, Fibrin degradation product; α 2PI, α 2 plasmin inhibitor. (From Kottke-Marchant K, Sapatnekar S. Hemostatic abnormalities in cardiopulmonary bypass: pathophysiologic and transfusion considerations. *Semin Cardiothorac Vasc Anesth*. 2001;5:187–206.)

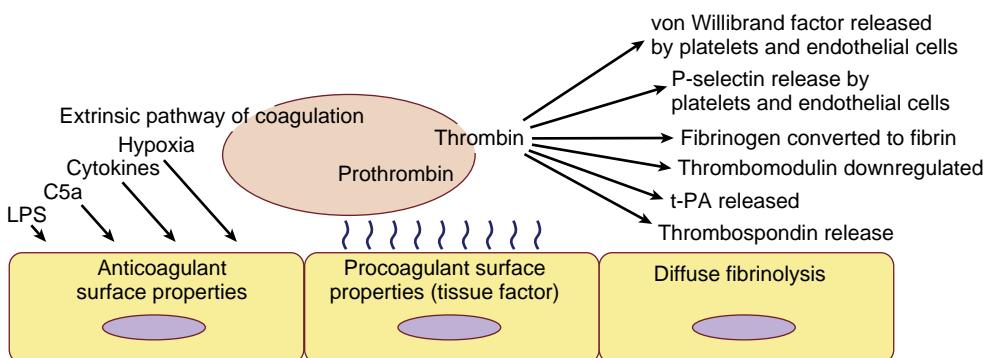


Fig. 54.9 Procoagulant endothelial cell activation. When endothelial cells are activated, they express tissue factor, which converts prothrombin to thrombin. Thrombin has multiple biologic actions: (1) stimulation of the release of von Willebrand factor and P-selectin, which cause platelet clumping and platelet, neutrophil, and endothelial cell adhesion; (2) conversion of fibrinogen to fibrin, the solid component of clot; (3) downregulation of the thrombomodulin/protein C and S systems; (4) release of tissue plasminogen activator (t-PA), which catalyzes the formation of plasmin; and (5) release of thrombospondin, which binds to t-PA, prevents its breakdown by plasminogen activator inhibitor-1 (PAI-1), and accelerates the formation of plasmin. LPS, Lipopolysaccharide. (From Boyle EM Jr, Verrier ED, Spiess BD. Endothelial cell injury in cardiovascular surgery: the procoagulant response. *Ann Thorac Surg*. 1996;62:1549-1557.)

an ACT of less than the target (400-480 seconds) after 600 to 800 units/kg of intravenous heparin are administered.⁹⁴ Others have defined heparin resistance as an ACT of less than 400 seconds at any time during the course of CPB and heparin administration.⁹⁵ Heparin resistance can result from a congenital deficiency or abnormality of AT, which requires treatment with AT to restore heparin's anticoagulant properties.⁹⁶ More often, however, heparin resistance is the result of an acquired condition caused by the patient's disease status and physiologic state. Giving these patients larger doses of heparin may augment the ACT value; therefore, a more accurate term for describing these clinical findings is altered heparin responsiveness. This alteration can result from an acquired AT deficiency, increased levels of heparin-binding proteins, activated platelets, sepsis, or other conditions. In a small study of cardiac surgical patients stratified by their history of preoperative heparin use, altered heparin responsiveness was found in approximately 40% of the patients who had received preoperative heparin therapy.⁹⁶

Reported risk factors for altered heparin responsiveness include AT levels less than 60% of normal, preoperative heparin therapy, and a platelet count greater than 300,000/ μ L. Ranucci and associates also found that low postoperative AT levels were predictive of a longer length of stay in the ICU,⁹⁷ and others have associated low AT levels with adverse myocardial outcomes.⁹⁸ Not all heparin resistance is AT mediated; thus, it is critical to understand the physiologic factors that contribute to the altered heparin responsiveness so that appropriate treatment can be instituted.⁹⁹⁻¹⁰¹

The most common treatment for altered heparin responsiveness is supplemental heparin. In refractory cases, treatment with AT concentrate, or recombinant AT, in doses that are calculated to produce 80% to 100% AT activity, restores heparin responsiveness. AT supplementation is a class I indication for heparin resistance that is due to AT deficiency.¹⁰² Thus the practice of replacing AT using this specific factor replacement is preferred over the use of plasma transfusion, which is no longer recommended due to the morbidity of allogeneic transfusion. When AT is used for this purpose, careful neutralization with protamine and

attention to hemostasis are essential because AT augments the effect of heparin and thereby slightly increases postoperative bleeding.¹⁰²

HEPARIN REBOUND. Heparin rebound is clinical bleeding that occurs within approximately 1 hour of protamine neutralization. It is accompanied by coagulation test results indicating residual heparinization, such as a prolonged partial thromboplastin time (PTT) or thrombin time and increased anti-factor Xa activity. Mechanisms of heparin rebound include slow dissociation of protein-bound heparin after protamine clearance, more rapid clearance of protamine than of heparin, lymphatic return of extracellular sequestered heparin, and the clearance of an unknown heparin antagonist. Heparin rebound is rare, yet it is more likely to occur when the protamine dose is based on the residual heparin concentration at the end of CPB than when protamine is given as a ratio to the total heparin administered, because using this ratio usually results in a slight "overdose." With coagulation monitoring, heparin rebound is easily prevented or treated with supplemental protamine. A protamine infusion has also been successful in preventing heparin rebound in patients in whom heparin rebound is a risk.¹⁰³ These include cases in which high doses of heparin were administered or in whom CPB time was prolonged. Perfusion management guidelines suggest that a low dose protamine infusion (25 mg/h) for up to 6 hours after the end of CPB may be considered as part of a multimodality blood conservation program (class IIb, Level of Evidence C).⁸²

HEPARIN-INDUCED THROMBOCYTOPENIA. HIT is an immune-mediated prothrombotic disorder that occurs in patients exposed to heparin. Antibodies form against the protein platelet factor 4 (PF4) when PF4 has formed a complex with heparin. Although PF4 is found in only trace amounts in human plasma and is stored in platelet α granules, the presence of heparin increases plasma PF4 concentrations 15- to 30-fold by displacing bound PF4 on endothelial cell surfaces. PF4 is also expressed on the surface membrane of activated platelets by membrane fusion with the α -granule membrane; thus, PF4 is exposed and available to bind with heparin. The resulting PF4-heparin complex on the platelet surface is recognized by a specific immunoglobulin G (IgG),

which binds to the complex and leads to immunologically mediated platelet activation. Hyperaggregability of these activated platelets is the hallmark of HIT and is responsible for its prothrombotic complications.^{104,105} Often a clinical score such as the 4 Ts score can be used to determine whether a heparin-platelet antibody test should be performed to diagnose HIT (class IIa, Level of Evidence B).⁸² Diagnosis can be difficult in the postcardiac surgery patient and often the 4 Ts score is unreliable.

A common presentation in patients with HIT is a reduction in the platelet count to less than 100,000/ μ L or to less than 50% of the baseline count. The incidence of seroconversion after CPB and heparin exposure is quite frequent (20%-50%).¹⁰⁶ However, the reported prevalence of clinical HIT after CPB is only 1% to 3%.¹⁰⁷ Thus, the risk of HIT in cardiac surgical patients with postoperative seroconversion is less than 10%.

The strength of the immunologic response, not the mere presence of PF4 or heparin antibodies, may determine which patients are prone to HIT and are at risk for thromboembolic complications.¹⁰⁷ The presence of preoperative antibody, in addition to postoperative antibody, has been associated with increased morbidity after cardiac surgery.¹⁰⁸ This morbidity takes the form of gut ischemia, renal dysfunction, limb ischemia, and other prothrombotic events.

Management of the cardiac surgical patient with HIT must include a careful risk-to-benefit analysis. The likelihood that a patient has true disease and is at increased risk for a thrombotic event must be weighed against the risks posed by using an alternative anticoagulant to heparin. The urgency of the surgical procedure is also an important factor that can affect decision making. It is preferable, when possible, to defer the operation until antibody titers have become undetectable⁸² or only weakly positive, which may occur after 90 days (class IIa, Level of Evidence C).¹⁰⁷ If surgical postponement is not practical, then other therapeutic options must be considered (Boxes 54.6 and 54.7). Currently, the direct thrombin inhibitors are used as the anticoagulants of choice. Hirudin and argatroban are approved by the U.S. Food and Drug Administration (FDA) for use in patients with HIT-related thrombosis.¹⁰⁹ The use of these drugs as anticoagulants for CPB is fraught with hemorrhagic complications. Bivalirudin has been approved by the FDA for use in percutaneous interventions and, because of its short half-life, has been favored as an anticoagulant for CPB in patients with HIT.¹¹⁰⁻¹¹² Guidelines suggest that in patients with a diagnosis of HIT and in need of an urgent operation requiring CPB, anticoagulation with bivalirudin is a reasonable option (class IIa, Level of Evidence B).⁸² However, no drug other than heparin has FDA approval for specific use as an anticoagulant in patients undergoing CPB. Bivalirudin undergoes renal elimination. Therefore, in seropositive HIT patients who have significant renal dysfunction, anticoagulation for urgent operations requiring CPB can be accomplished with argatroban, plasmapheresis prior to heparin to remove antibodies, or heparin with concomitant antiplatelet agents to prevent platelet activation (tirofiban, iloprost) (class IIb, Level of Evidence C).⁸² These latter two techniques have risk because they include heparin, and have been fraught with increased risks of bleeding. Boxes 54.6 and 54.7 summarize therapeutic options and

BOX 54.6 Therapeutic Options for Anticoagulation for Cardiopulmonary Bypass in Patients With Heparin-Induced Thrombocytopenia

1. Ancrod
 2. Low-molecular-weight heparin or heparinoid (test first)
 3. Alternative thrombin inhibitor (hirudin, bivalirudin, argatroban)
 4. Using a single dose of heparin, promptly neutralizing it with protamine, and
 - a. Delaying surgery so antibodies can regress or
 - b. Using plasmapheresis to decrease antibody levels or
 - c. Inhibiting platelets with iloprost, aspirin and dipyridamole (Persantine), abciximab, or RGD blockers
- In all cases:
1. No heparin in flush solutions
 2. No heparin-bonded catheters
 3. No heparin lock intravenous ports
- No agent is currently indicated for anticoagulation in cardiopulmonary bypass.

RGD, Receptor glycoprotein-derived.

Modified from Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:966.

BOX 54.7 Potential Alternative Anticoagulants for Cardiopulmonary Bypass

- Ancrod
- Low-molecular-weight heparins
- Factor Xa inhibitors
- Bivalirudin or other direct thrombin inhibitors (hirudin, argatroban)
- Platelet receptor inhibitors

From Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:967.

alternative anticoagulant strategies for the patient with HIT whose operation cannot be deferred until seronegativity is documented. Fig. 54.10 delineates how each alternative drug inhibits factor Xa, thrombin, or fibrinogen.

Protamine Reactions. Protamine is associated with several hemodynamic effects that can be categorized by their presentation and mechanism. Adverse reactions to protamine range from moderate hypotension to more profound and hemodynamically significant reactions that can increase in-hospital mortality risk.^{113,114} The clinical presentation of these reactions serves as a starting point for understanding their mechanistic relationships. Commonly, these reactions are classified as type I, type II, or type III. A type I protamine reaction involves isolated hypotension, with normal to low filling pressures and normal airway pressures. This reaction is usually mild and responds to volume infusion, slowing of protamine infusion, and the gentle titration of vasoactive medications. Type II reactions include moderate to severe hypotension and features of anaphylactoid reactions, such as bronchoconstriction. Anaphylactoid reactions include protamine sensitivity reactions that are classically immunologic or allergic in that they are immunoglobulin E (IgE) antibody mediated. Nonimmunologic mechanisms may involve IgG antibodies

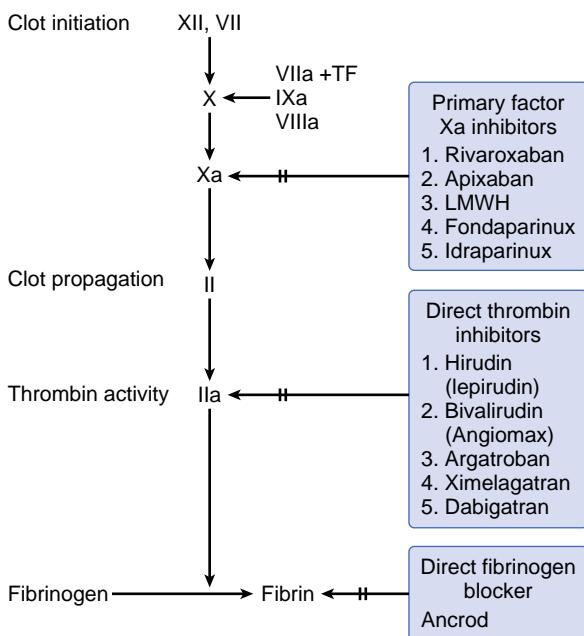


Fig. 54.10 Alternatives to heparin. Newer anticoagulants are shown in the boxes on the right side of the figure; these drugs inhibit factor Xa, thrombin, or fibrinogen. LMWH, Low-molecular-weight heparin; TF, tissue factor. (From Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:968.)

or complement activation. Type III reactions are thought to be caused by large heparin-protamine complexes that lodge in the pulmonary circulation, cause the release of mediators, and result in severe hypotension and elevated PA pressures that may lead to acute RV failure. This is obviously a profound response, resulting in global cardiovascular collapse or necessitating the reinstatement of CPB because of intractable RV failure. Fortunately, catastrophic hypotension and intractable RV failure are relatively rare events on the spectrum of protamine reactions.¹¹³

Mechanistic explanations for protamine reactions include endothelial nitric oxide release, mast cell degranulation, and histamine release associated with rapid infusion. A study by Kimmel and colleagues found that neutral protamine Hagedorn insulin use, documented fish allergy, and a history of nonprotamine medical allergies were independent risk factors for protamine hypersensitivity reactions.¹¹⁵ In this study, 39% of patients who presented for cardiac surgery had one or more of these risk factors. Other possible but unconfirmed risk factors include prior exposure to protamine, a history of vasectomy, decreased LV function, and hemodynamic instability.¹¹⁵ The site of injection does not influence the incidence of protamine reactions.¹¹⁶ Pretreatment with histamine blockade is not preventive.

The following principles summarize treatment options for patients at risk for protamine reactions:

1. Protamine should be administered slowly (i.e., over ≥ 5 minutes). Limit protamine dose to less than 2.6 mg protamine/100 units of heparin, since total doses above this ratio inhibit platelet function, prolong ACT, and increase the risk of bleeding (class IIa, Level of Evidence C).⁸²
2. In patients with documented adverse events related to protamine, consideration should be given to *not* rechallenging the patient with protamine. Pharmacologic

alternatives to protamine can be considered, or a decision can be made not to reverse heparin. Consideration may be given to using non-heparin-based CPB, performing off-pump coronary artery bypass (OPCAB) with an alternative to heparin, or, if heparin is used, administering nonprotamine heparin reversal drugs such as heparinase, or simply waiting for heparin's effects to dissipate.

3. Hypotension associated with protamine reversal of heparin often is ameliorated by simply slowing or pausing protamine infusion while volume is infused through intravenous lines or the aortic cannula. Vasoactive medications, such as phenylephrine or ephedrine, use of calcium chloride, or increased inotropic support may be necessary.
4. Severe or intractable hypotension, with or without evidence of pulmonary circulatory involvement, bronchospasm, or overt RV failure, demands immediate aggressive attention, intervention, and planning for a potential return to CPB. Steps to consider include the following:
 - a. Reheparinization to prepare the patient for a return to CPB and to reduce heparin-protamine complex size. If hemodynamics permit, a low dose of heparin (70 units/kg) may be tried first while supportive treatment continues, followed by a full CPB dose of heparin (300 units/kg) if it becomes necessary to return the patient to CPB. (class I, Level of Evidence C).⁸²
 - b. Inotropic support, either by infusion or by intermittent bolus administration, is warranted. Epinephrine and norepinephrine are acceptable options, and milrinone may be considered if the patient's hemodynamic status permits.
 - c. If the patient's hemodynamic status allows, nebulized albuterol is helpful in the management of bronchospasm and elevated airway pressures.

Antifibrinolytic Therapy: Prophylaxis for Bleeding. Prophylactic use of antifibrinolytic drugs before CPB reduces bleeding and transfusion requirements in cardiac surgical patients in randomized trials and in multiple meta-analyses.^{117,118} The most well-known antifibrinolytic drugs include the synthetic lysine analogues ϵ -aminocaproic acid (EACA) and tranexamic acid (TA) and the serine protease inhibitor aprotinin. Presumably, the blood-sparing effects of the synthetic drugs result from the inhibition of fibrinolysis by their binding to the lysine-binding sites on plasmin. This also has platelet protective properties because plasmin's antiplatelet effects are also inhibited by antagonist binding.

Aprotinin is a direct enzymatic inhibitor of plasmin and has other protease-inhibiting properties that confer its antiinflammatory and antikallikrein effects. However, aprotinin was notably associated with increases in post-CPB creatinine values and other adverse organ system outcomes in large-scale observational trials.¹¹⁹ When a randomized prospective trial showed an increase in mortality in the aprotinin group, despite a reduction in bleeding, the drug was removed from the global market.¹²⁰ Although the causes of death in the aprotinin-treated patients were not found to be related to thrombosis or other drug-related effects, aprotinin was rendered unavailable for commercial use for years after publication of this study. The decision to

remove aprotinin from clinical use was revisited on reevaluation of these study data, and aprotinin has been reintroduced in Canada and other countries specifically for use as labeled in CABG surgery.

Hypercoagulable States. The use of antifibrinolitics has become common in cardiac operations that require CPB. The use of antifibrinolytic drugs and prohemostatic drugs and blood products to treat bleeding has brought to light the risk of thrombosis in CPB, during which feedback mechanisms are critical and homeostasis is perturbed. All patients incur this risk of thrombosis as consumptive coagulopathy increases, but the risk is greatly increased in patients with congenital or acquired thrombophilic states.¹²¹ These states may be important in view of current practices that involve pharmacologically inhibiting fibrinolytic pathways in cardiac surgical patients.

The factor V Leiden (FVL) mutation is the most common inherited thrombophilic disorder; its prevalence is 3% to 7% in white populations.^{122,123} Mechanistically and clinically, FVL has been implicated in thrombotic complications in cardiac operations, most often those involving a period of circulatory arrest and the use of antifibrinolitics.¹²⁴ In a review of FVL mutation, Donahue gave the following summation and recommendations¹²¹:

- Cardiac surgical patients who are heterozygous for the FVL mutation bleed less than do noncarriers.
- The risk of early graft thrombosis may be increased in patients with FVL deficiency.
- The use of antifibrinolytic drugs may increase thrombotic risk in patients with FVL.
- Anecdotal evidence suggests that in patients with FVL mutation who are exposed to deep hypothermic circulatory arrest, antifibrinolitics increase thrombotic risk.

Cardiac Surgical Patients Taking Anticoagulant or Antithrombotic Drugs.

Antithrombotic therapy in cardiac surgical patients has many roles and applications. Patients with ischemic heart disease can be managed short- or long-term with pharmacologic drugs that may include aspirin, AT inhibitors (heparins), direct thrombin inhibitors, or an array of platelet inhibitors (adenosine diphosphate [ADP] receptor inhibitors and glycoprotein IIb/IIIa [Gp IIb/IIIa] receptor inhibitors). Patients with a history of peripheral vascular disease, valvular heart disease, or low ventricular ejection states can similarly be managed with some form of antithrombotic therapy that may also include warfarin. Frequently, patients arrive for surgery while receiving multiple antithrombotic medications. Thus, postoperative bleeding is a common but challenging complication of cardiac surgery, especially when the bleeding risk posed by CPB itself is considered.

The use of percutaneous coronary interventions such as angioplasty and intracoronary stent deployment for ischemic heart disease has led to the use of antithrombotic medications to maintain stent patency and to prevent stent thrombosis. The American College of Cardiology and AHA (ACC/AHA) initial guidelines for percutaneous coronary intervention recommended (on the basis of class I evidence) the use of both aspirin and clopidogrel for at least 1 year after drug-eluting stent placement.¹²⁵ However,

percutaneous coronary intervention data with the second generation drug-eluting stents indicate that shorter periods of dual anti-platelet therapy are equally effective in preventing in-stent thrombosis, and thus allow for earlier cessation of a single anti-platelet agent after 6 months.¹²⁶ This opens the door for interventions and surgical procedures to be performed sooner and with less risk of bleeding. The administration of thienopyridine antiplatelet drugs in addition to aspirin increases the risk of bleeding after cardiac surgery¹²⁷; however, it is unclear whether aspirin alone increases this risk. Abundant evidence (mostly level B evidence from small, retrospective, nonrandomized studies) suggests that the ADP receptor antagonist clopidogrel (Plavix) has been associated with excessive perioperative bleeding in patients who undergo CABG.¹²⁸ This trend has even been reported in the OPCAB population, although not consistently.¹²⁹ Earlier recommendations included a 5- to 7-day delay after discontinuation of clopidogrel in patients who require CABG. However, guidelines⁷⁷ suggest that a 3-day delay may be sufficient to lessen bleeding risk and provide safe outcomes.¹³⁰ It is likely that a 5- to 7-day delay is not necessary, but some interval between the discontinuation of clopidogrel and CABG is supported by the available evidence.

Patients with a history of Gp IIb/IIIa receptor blockade as a part of their acute coronary syndrome management are at risk of increased bleeding and blood component use when they are given abciximab, especially within 12 hours of cardiac surgery.^{131,132} Shorter-acting Gp IIb/IIIa receptor antagonists do not seem to increase bleeding or adverse outcomes and in fact may improve myocardial outcomes when Gp IIb/IIIa blockers are in use.¹³³ The interval between the discontinuation of antiplatelet therapy and cardiac or noncardiac surgery is critical to preventing thrombotic events without increasing the risk of bleeding. These decisions regarding the cessation of therapy can be guided by knowledge of drug pharmacology and testing of antiplatelet drug efficacy.

Enoxaparin, a low-molecular-weight heparin, increases transfusion rates and the risk of surgical reexploration when it is used in association with CPB.¹³⁴ Low-molecular-weight heparin may also decrease heparin responsiveness.¹³⁵

Patients who present for cardiac surgery with residual warfarin effects may benefit by having enhanced anticoagulation during CPB. Postoperatively, if excessive bleeding is noted and is confirmed by hemostasis testing, factor replacement can be performed with blood products or pharmacologic prothrombin complex concentrates (PCCs).

Patients with atrial fibrillation may be maintained on new antithrombotic therapeutic drugs, direct oral anticoagulants (DOACs) that include thrombin inhibitors (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban). These drugs are potent and long-acting, and they have no antidote, so one would expect that treating cardiac surgical patients with these drugs would increase their bleeding risk. When compared to vitamin K antagonists, the DOACs have similar thromboprophylaxis efficacy yet fewer bleeding complications.¹³⁶ An additional benefit is that DOACs have a predictable pharmacodynamic profile and routine monitoring is often unnecessary. Routine monitoring tests such as the INR and aPTT do not even accurately assess anticoagulant activity of the DOACs and

thus a thrombin time or a direct measure of anti-Xa activity would be considered more accurate.^{137,138}

In summary, patients who present for cardiac surgery with preexisting, pharmacologically induced inhibition of the hemostatic system may have undesirable post-CPB bleeding. The diagnosis and treatment of this complication should be the same whether the derangement is a function of CPB itself, coexisting pharmacologic inhibition, or both. The management and treatment of persistent postoperative bleeding are discussed in the section on problems in the postoperative period.

INDUCTION OF ANESTHESIA AND THE PREBYPASS PERIOD

Premedication

The anesthesiologist should ensure that appropriate premedications are administered with a sip of water on the morning of surgery. With a few exceptions, patients should receive their usual long-term medications, particularly β -adrenergic blocking drugs, on the day of surgery. The clinician should be aware that ACE inhibitors (ACEIs), if administered on the day of surgery, may increase the patient's propensity for hypotension.¹³⁹ With respect to aspirin, it is recognized that aspirin administration in the early postoperative period may reduce the risk of ischemic complications after CABG surgery.¹⁴⁰ However, patients who receive aspirin immediately preoperatively may have more mediastinal bleeding and greater transfusion requirements. A consensus statement published by the STS recommends that low-intensity antiplatelet drugs (e.g., aspirin) be discontinued before cardiac surgery to reduce patients' blood transfusion requirements, but this should be done only in purely elective cases in patients without acute coronary syndromes.⁷⁶

However, drugs that inhibit the platelet P2Y12 receptor should be discontinued before operative coronary revascularization (either on-pump or off-pump), if possible.⁷⁶ The interval between drug discontinuation and operation is determined from the drug's pharmacodynamics but may be as short as 3 days for irreversible inhibitors of the P2Y12 platelet receptor. POC tests are available to measure platelet ADP responsiveness. POC tests that show normal platelet ADP responsiveness after administration of an initial dose of clopidogrel indicate P2Y12 resistance with as much as 85% specificity.^{141,142} This is called "high on-treatment platelet reactivity." Flow cytometry may be more specific in diagnosing the degree of platelet inhibition, but it cannot be measured at the point of care.^{141,143}

The prospect of undergoing cardiac surgery provokes anxiety in most patients. Furthermore, the insertion of intravenous and arterial catheters is painful and must be done before anesthesia is induced. The resultant anxiety and pain can lead to undesirable sympathetic stimulation, with consequent tachycardia and hypertension. The first step in preventing this cycle is thoroughly explaining the anticipated anesthetic techniques and procedures to the patient. Premedication with a narcotic or anxiolytic drug, or both, to mitigate pain and anxiety is usually indicated before the patient is transported to the operating suite. Supplemental intravenous drugs—commonly midazolam and possibly fentanyl—are usually necessary during radial

artery cannulation before anesthesia is induced. However, in patients with low CO secondary to congestive HF (CHF), sedation should be performed judiciously to avoid myocardial depression and resultant hypotension. Moreover, in patients with significant pulmonary hypertension, oversedation and respiratory depression leading to hypercapnia or hypoxia must be avoided.

Induction of Anesthesia

In preparing for induction, the clinician should have the following drugs immediately available: vasopressors (e.g., phenylephrine, ephedrine, calcium chloride, readily available vasopressin), one or more inotropes (e.g., ephedrine; epinephrine; readily available norepinephrine, dopamine, or dobutamine), one or more vasodilators (e.g., nitroglycerin, nitroprusside, nicardipine), an anticholinergic drug (atropine), antiarrhythmic drugs (e.g., lidocaine, esmolol, magnesium, amiodarone, adenosine), and heparin.¹⁴⁴ Commonly administered drugs should be drawn up and ready for administration by bolus or infusion, as appropriate; agents that are used less commonly should be readily available in the operating room. Protamine should be readily available, but many institutions require that protamine be stored in unique packaging or at a separate, nearby location to prevent inadvertent premature administration.

Furthermore, the selected antibiotic should be ready to administer according to Surgical Care Improvement Project guidelines. The STS recommends a cephalosporin as the primary prophylactic antibiotic for cardiac surgery; the drug should be administered within 1 hour before incision.¹⁴⁵ In patients who are allergic to penicillin, vancomycin is administered within 2 hours of incision. Finally, antifibrinolytic drugs are commonly used to minimize bleeding and the need for transfusion during cardiac surgery. The most commonly used antifibrinolytic drugs are the synthetic lysine analogues TA and EACA; both reduce total blood loss and decrease the number of patients who require blood transfusion during cardiac procedures.⁷⁶

Anesthetic drugs and techniques for inducing anesthesia should be selected with consideration of the patient's cardiac pathophysiology and other comorbid conditions. No single "recipe" can guarantee hemodynamic stability during anesthetic induction. Hypotension may result in a patient who is relatively hypovolemic and receives a vasodilator or whose sympathetic tone is reduced by anesthesia. Hypotension is particularly common in patients with poor LV function. Conversely, in patients with good myocardial function, hypertension may occur during induction because of preinduction anxiety or sympathetic stimulation caused by laryngoscopy and endotracheal intubation.

The radial artery or an alternative site should be cannulated before induction of anesthesia to monitor arterial pressure on a beat-to-beat basis. If the radial artery is being harvested as a vascular conduit, the contralateral radial or brachial artery or a femoral artery can be cannulated. Basic monitors, including the ECG and pulse oximeter, should also be used during the induction of anesthesia. During any cardiac surgical procedure, central venous access is necessary to secure so that volume infusion, transfusion therapy, and vasoactive drug administration can be easily delivered directly to the central circulation. A central venous catheter or a PA catheter can be placed either before or after

anesthesia is induced. Placement before anesthesia induction is ideal so that the CVPs can be monitored during the induction of anesthesia. However, the placement of these lines in the awake patient can take more time and create discomfort, thus causing unwanted hypertension and tachycardia. The risk-benefit analysis usually dictates that the central venous line be placed after anesthesia induction. The urinary bladder catheter, nasogastric tube, TEE probe, and any additional temperature monitors (e.g., a nasopharyngeal probe) are positioned after induction of anesthesia.

When choosing anesthetic drugs and doses during induction and maintenance, one should consider any pharmacodynamic properties that could affect arterial blood pressure, heart rate, or CO, as well as the desirability of “early” extubation of the trachea (i.e., within a few hours after the operation is completed). Anesthesia is most commonly induced with an opioid and a sedative-hypnotic (etomidate, thiopental, propofol, or midazolam). All anesthetics decrease arterial blood pressure by decreasing sympathetic tone, decreasing systemic vascular resistance (SVR), inducing bradycardia, or directly depressing myocardial function. The only exception is ketamine, which has sympathomimetic effects; however, in patients with catecholamine depletion, ketamine’s sympathomimetic effects may not counterbalance its direct negative inotropic effects. Because of their pharmacologic complexities, all anesthetic agents should be administered judiciously in patients who are critically ill or who have poor LV function.

Muscle relaxants are usually given early in the sequence of anesthetic induction, particularly if relatively large doses of opioids are administered, to minimize chest wall rigidity (see also Chapter 27). With the routine use of fast-track anesthesia techniques, including a trend toward earlier extubation, volatile anesthetics are often chosen as the primary maintenance anesthetic. The predominant effect of isoflurane, desflurane, and sevoflurane is dose-dependent vasodilation with resultant decreases in SVR and arterial blood pressure. These volatile anesthetics may have an advantage in inducing preconditioning, which is particularly important in patients undergoing either CABG with CPB or OPCAB, in which myocardial ischemic insults are likely. The volatile anesthetic agents have several cardioprotective effects, including triggering the preconditioning cascade and mitigating reperfusion injury.¹⁴⁶ However, nitrous oxide probably should be avoided because it can increase gaseous bubble size and adversely affect pulmonary vascular resistance (PVR).

The Pre-Cardiopulmonary Bypass Period

After anesthesia is induced, several important details must be remembered, especially positioning (see also Chapter 34). Methods of positioning the arms vary according to institutional practice, but one must avoid causing brachial plexus injury by hyperextending the arms, ulnar nerve injury by improperly padding the olecranon, radial nerve injury by compressing the upper part of the arm against the sternal retractor support posts, or finger injury by entrapping the finger against the metal edge of the surgical table. Proper positioning also ensures that arterial catheters previously placed in the radial, ulnar, or brachial arteries are not “damped.” The head should be padded and occasionally repositioned during the procedure to prevent occipital

alopecia, which can occur several days postoperatively. The eyes should be taped, possibly lubricated, and definitely free from pressure. Pressure-related injury to any soft tissue will potentially be exacerbated by hypothermia and decreased perfusion during CPB. All monitors and tubing should be checked after final positioning to ensure that none are kinked, entrapped, tangled, or inaccessible. Additionally, antibiotics must be administered (with documentation) within 1 hour of incision (vancomycin within 2 hours). Arterial blood gases and blood chemistry (electrolytes, glucose, and calcium), as well as baseline ACT, should be measured shortly after anesthesia is induced. If a continuous mixed venous PA catheter has been inserted, mixed venous hemoglobin oxygen saturation should be measured to calibrate the device.

During the prebypass period, the anesthesiologist’s main goal is to maintain the hemodynamic and metabolic stability of the patient while making preparations for CPB. The degree of surgical stimulation varies markedly during this period. Positioning the patient, inserting additional monitors, preparing the skin, and harvesting the saphenous vein or veins cause only minimal sympathetic stimulation. Therefore, hypovolemic patients and those with poor ventricular function may be susceptible to hypotension during these periods. In contrast, chest incision, sternal splitting, and harvesting of the IMA involve more intense surgical stimulation. These events may cause hypertension, tachycardia, and dysrhythmias, even in previously hypotensive patients. However, just before CPB is initiated, during the cannulation of the great vessels, surgical stimulation is again minimal, and manipulation of the heart and great vessels may transiently decrease venous return and cause a precipitous decline in blood pressure. The anesthesiologist must be ready to treat all hemodynamic aberrations with the vasopressor, inotropic, vasodilator, antiarrhythmic, and anticholinergic drugs mentioned earlier.

In preparation for CPB, anticoagulation must be achieved. Heparin is still the standard drug used and is administered through a central venous catheter at an initial dose of 300 to 400 units/kg. The onset of anticoagulation is almost immediate, but generally, the drug is allowed to circulate for 3 to 5 minutes before its effect is measured. The ACT must increase to at least 300 seconds before CPB is initiated, although most institutions use at least 400 seconds as their standard. Additional heparin is administered, if necessary, to increase the ACT to the desired level. Subsequently, it is common to administer an antifibrinolytic drug (EACA or TA) in an attempt to minimize bleeding and the need for transfusion during cardiac surgery.

After heparinization, the next major step in the prebypass phase is vascular cannulation. One or more large veins or the right atrium is cannulated so that all systemic venous blood is diverted to the pump oxygenator. Additionally, a large artery, usually the ascending aorta, is cannulated so that oxygenated blood is delivered back to the arterial circulation. Heparin is always administered before cannulation. Usually, arterial cannulation is established before venous cannulation to allow rapid intravascular volume or blood resuscitation if necessary. Complications of aortic cannulation include arterial dissection, hemorrhage and resultant hypotension, inadvertent cannulation of the aortic arch vessels, and embolic phenomena caused by dislodged

atherosclerotic plaque or by air introduced into or entrained around the aortic cannula. Complications of venous cannulation include hypotension from blood loss, dysrhythmias, and surgical mechanical compression of the heart or great vessels. When arterial cannulation is successful and the cannula has been inspected to ensure that no air is present, volume can be administered in 100-mL increments to treat bleeding and hypovolemia. If necessary, dysrhythmias are treated by cardioversion, medications, or rapid initiation of CPB.

Patients undergoing redo cardiac surgery (i.e., those who have previously had a median sternotomy) warrant special concern about the possibility of sudden, massive hemorrhage. At least 2 units of blood should be immediately available for all redo cases. Frequently, the surgeon will elect to use an oscillating saw in these patients, but mediastinal structures adherent to the underside of the sternum may nevertheless be injured. If the right atrium, right ventricle, great vessels, or an existing coronary graft is cut, the surgeon may elect to initiate CPB on an emergency basis. Therefore, the anesthesiologist should have a systemic dose of heparin prepared. As soon as the patient is heparinized, the femoral or aortic arterial cannula is inserted, and the cardiotomy suckers can be used to create venous return (so-called sucker bypass).

Onset of Cardiopulmonary Bypass

Preparing for the onset of CPB brings about a new set of challenges for a cardiac anesthesiologist. As a preparation for CPB, the surgeon would start by placing purse string sutures in the ascending aorta for the eventual placement of aortic cannula. It is imperative that at this point the anesthesiologist keeps the patient's blood pressure in a range that would not jeopardize the integrity of the aorta while the cannula is placed. A systolic blood pressure of 90 to 110 mm Hg is traditionally accepted for this stage of the procedure. Around this time heparin will also be administered. Usually 300 units/kg patient weight is administered for a target ACT of 450 to 500 seconds, to safely start the CPB. After the safe placement of aortic cannula, remaining cannulas will be placed by the surgeon, followed by start of the CPB.

During the abovementioned process, a cardiac anesthesiologist monitors the patient's hemodynamics and rhythm for any undesired changes.

With the onset of CPB, to guard against malposition of the aortic or venous cannula, the perfusionist checks the aortic inflow line pressure and for signs of inadequate venous return while the anesthesiologist checks for persistently low arterial pressure, unilateral blanching of the face, or any swelling in the neck veins, face, or conjunctiva. Once full bypass is established and aortic ejection by the heart has ceased, ventilation and inhaled drugs can be discontinued. If a PA catheter is present, it is pulled back 3 to 5 cm to minimize the risk of pulmonary perforation as the pulmonary arteries collapse. Prebypass urine output is recorded and emptied so that urine output during CPB can be monitored separately. The TEE probe may be used to watch for LV distention with the onset of CPB, which may indicate aortic valve regurgitation or other hemodynamic problems. Once CPB is established, the probe is left in the unlocked (neutral) position until the

cardiac chambers are de-aired and the patient is weaned from CPB.

To ensure adequate anesthetic depth, supplemental intravenous sedative-hypnotics are administered, or a volatile agent is administered through a vaporizer connected to the oxygenator gas inlet of the CPB circuit. Administration of muscle relaxant is continued to prevent spontaneous ventilation, movement, or shivering during hypothermia and rewarming.

WEANING FROM CARDIOPULMONARY BYPASS

After the completion of surgery on CPB, the patient is prepared for coming off of the CPB and the resumption of patient's own physiology.

As part of a cardiac anesthesiologist's responsibilities it is of paramount importance that a plan is made beforehand for this part of cardiac surgery. The plan should take into account the nature of surgery, the length of bypass run, length of the aortic cross clamp and patient's presurgical cardiac status and comorbidities.

In preparation of weaning the patient off of the CPB several issues need to be addressed before a successful weaning process is started. Issues that need to be addressed include temperature, electrolytes (specifically potassium), rhythm, systemic blood pressure, contractility, and any air in the left ventricle (LV).

After addressing the abovementioned issues, the perfusionist gradually allows more and more blood to be pumped by the heart instead of the bypass machine. During this time the cardiac anesthesiologist ensures that any inotropic and/or volume requirements of the patient are met to successfully bring the CPB run to its conclusion.

The "CVP" Mnemonic

Fortunately, for most patients, separation from CPB is a relatively uneventful process. A review by Licker and colleagues emphasized that the key to successful weaning from bypass is clear communication among members of the operating room team.¹⁴⁷ In a study conducted at the Mayo Clinic in Rochester, Minnesota,¹⁴⁸ a strong correlation was noted between the frequency of technical errors and poor communication or coordination among the surgeon, anesthesiologist, and perfusionist.

Regarding clinical issues, several criteria should be met in all cardiac surgical cases before weaning from CPB is attempted. Morris and colleagues suggest a mnemonic, "CVP," to help the clinician remember the main tasks necessary for the successful termination of CPB (Table 54.4).¹⁴⁹ Each letter of CVP represents several tasks or important points to remember that begin with that letter.

The first "C" stands for cold, which refers to the patient's temperature at the time of weaning from CPB, which should be 36°C to 37°C. Neither the temperature of the venous blood returning to the CPB circuit nor the nasopharyngeal temperature should ever exceed 37°C because hyperthermia may increase the risk of postoperative neurologic complications (see the section on "Temperature").

The second "C" stands for conduction, which refers to cardiac rate and rhythm. A heart rate of 80 to 100 beats/min is usually desirable. Bradycardia is treated with epicardial pacing wires and/or with β-adrenergic drugs that have

chronotropic and dromotropic, as well as inotropic, properties. Tachycardia (i.e., heart rate >120 beats/min) is also undesirable. Sinus tachycardia may result from anemia, hypovolemia, “light” anesthesia, or the administration of chronotropic drugs; treatment is tailored to the presumed cause. Rhythm is also an important factor in optimizing CO. Third-degree AV block requires pacing, ideally AV pacing. Sinus rhythm is preferable, particularly in patients with poor LV compliance, who are especially dependent on an “atrial kick” to achieve adequate filling. If supraventricular tachycardia is present, direct synchronized cardioversion is often warranted. In addition, pharmacologic therapy with amiodarone, esmolol, verapamil, or adenosine may be used in the initial treatment of or to prevent the recurrence of supraventricular tachycardia.

The third “C” stands for CO or contractility. Contractility may be estimated from TEE or PA catheter data, if available.

The fourth “C” refers to cells (i.e., red blood cells [RBCs]). The patient’s hemoglobin concentration should be 7 to 8 g/dL, or slightly higher, before weaning from CPB. If the hemoglobin concentration is less than 6.5 g/dL when rewarming commences, the perfusionist and anesthesiologist can consider hemoconcentration or transfusion of a unit of packed RBCs (PRBCs).

The fifth “C” refers to calcium, which should be immediately available for possible administration to treat hypocalcemia and hyperkalemia. Ionized calcium levels should be measured after rewarming to help direct therapy. Although calcium is not administered routinely, if ionized calcium levels are in the low-normal range, SVR can be beneficially increased by calcium administration.

The sixth “C” stands for coagulation. After protamine is administered, ACT is measured. In patients at risk for coagulation abnormalities, prothrombin time, PTT, and platelet count should also be measured a few minutes later. If POC coagulation monitoring such as the viscoelastic tests are available, these should be measured at this time. Examples of patients at risk for coagulation abnormalities include the following: those with long CPB times; those with extreme hypothermia, elective circulatory arrest, or both, during CPB; and those with chronic renal failure. Platelet function tests may be useful in patients taking platelet inhibitors (e.g., clopidogrel or aspirin). (For further discussion of patients having emergency surgery who are taking warfarin or who have been exposed to thrombolytic drugs, anti-platelet Gp IIb/IIIa agents, or direct thrombin inhibitors see the sections on the “hematologic system” and on bleeding and coagulopathy.)

The first “V” stands for ventilation of the lungs. As CPB is discontinued, the venous outflow line is gradually occluded, and PA blood flow is gradually restored. Pulmonary ventilation and oxygenation must be reestablished, thus allowing the lungs to become the site of gas exchange again. Ideally, the lungs are initially reinflated manually, with a few sustained inflations to a peak pressure of approximately 30 cm H₂O. If an IMA has been grafted to a coronary artery, the anesthesiologist must examine the surgical field during these inflations to ensure that the grafted artery is not overstretched, which could disrupt the distal anastomosis. Additionally, the compliance of the lungs is judged by these initial inflations, and bronchodilators can be administered if necessary. The surgeon

should remove any fluid or blood from the pleural spaces and ensure that any pneumothorax is treated with a chest tube.

The second “V” refers to visualization of the heart, both directly in the surgical field (where the right-sided chambers are visible) and on the TEE, to estimate global and regional contractility. Furthermore, the degree of chamber filling (hypovolemic, euvolemic, or distended) can be estimated. In addition, one can do a final check for air within the cardiac chambers with TEE examination.

The third “V” stands for vaporizer, meaning that if volatile agents were used to ensure lack of awareness or to control blood pressure during CPB, the clinician usually reinstutes a low dose immediately after weaning. However, because all the volatile agents decrease contractility and blood pressure, these effects can confuse the differential diagnosis of hypotension and myocardial dysfunction during weaning.

The final “V” refers to volume expanders. When all products from the pump have been exhausted and if blood transfusion is not indicated, crystalloid and albumin or hetastarch should be readily available to increase preload rapidly if necessary.

As for the letter “P” in the CVP mnemonic, Morris et al. explained that the first task “P” represents the need to be aware of predictors of adverse cardiovascular outcome.¹⁴⁹ For example, preoperative low EF and prolonged CPB often predict difficulty in weaning the patient from CPB and the need for inotropic support. In addition, emergency surgery in patients with acute coronary syndrome may lead to myocardial stunning. Furthermore, inadequate surgical repair (e.g., incomplete coronary revascularization) may result in ongoing ischemia.

The second “P” stands for pressure. Calibration and rezeroing are accomplished shortly before the patient begins being weaned from CPB. Any discrepancy between the distal (usually radial) arterial pressure and the central aortic pressure should be recognized. Occasionally, the surgeon may need to insert a temporary aortic root cannula or a longer-lasting femoral arterial cannula to monitor systemic blood pressure accurately during and after the termination of CPB.

The third “P” refers to pressors, meaning vasopressors and inotropic agents that should be immediately available. A vasodilator, such as nitroglycerin, nicardipine, or nitroprusside, also should be immediately available.

The fourth “P” represents pacer because an external pacemaker should be readily available for all patients. Pacing is often needed to treat bradycardia. In patients with heart block, ideally, an AV sequential pacemaker is used to maintain the atrial kick.

The fifth “P” stands for potassium because hypokalemia may contribute to dysrhythmias, and hyperkalemia may result in conduction abnormalities. In addition, the patient’s ionized calcium level is usually checked; most clinicians have a low threshold for administering additional calcium chloride. Furthermore, magnesium (2-4 g) is usually administered before CPB is terminated. Although magnesium’s efficacy in preventing postoperative atrial or ventricular dysrhythmias has not been clearly demonstrated, hypomagnesemia is common after CPB. The risk-to-benefit ratio for administering a 2- to 4-g dose is low.

TABLE 54.4 Elements of Morris, Romanoff, and Royster's "Central Venous Pressure" Mnemonic for Weaning Patients from Cardiopulmonary Bypass

C	V	P
Cold	Ventilation	Predictors
Conduction	Visualization	Pressure
Cardiac output	Vaporizer	Pressors
Cells	Volume expanders	Pacer
Calcium		Potassium
Coagulation		Protamine

From Morris BN, Romanoff ME, Royster RL. The postcardiopulmonary bypass period: weaning to ICU transport. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:230–260.

The final "P" refers to protamine. Many institutions require that protamine be uniquely packaged or kept in a nearby but separate area to ensure that the drug is not prematurely administered. (Administration during ongoing CPB is a disastrous error.) Nevertheless, it should take but a few moments to retrieve protamine when the surgeon, anesthesiologist, and perfusionist agree that it is time to reverse anticoagulation.

TERMINATION OF CARDIOPULMONARY BYPASS

After all the preparations described previously have been made and the patient's ventilation has been reestablished, the venous return to the pump is reduced by gradually clamping the venous line. The patient's intravascular volume is carefully increased by continued inflow through the aortic or other arterial cannula. Ventricular distention should be avoided because it increases wall tension and myocardial oxygen consumption. The pump flow into the aorta is lowered, in effect moving into a "partial bypass" phase, in which some of the venous blood still goes into the pump and some passes through the right ventricle and lungs to be ejected into the aorta by the LV. Some clinicians reduce the pump flow to half flow rather than gradually reducing venous return to the pump. Once loading conditions are optimal and contractility appears adequate, the aortic inflow line may be clamped to separate the patient from CPB.

If CPB has been successfully terminated but cardiac performance is not optimal, preload can be increased by infusing additional blood from the pump into the aortic cannula, usually in 100-mL increments in adult patients. Monitoring the left intraventricular volume in a qualitative fashion by TEE, observing the right ventricle directly, and monitoring the filling pressures give a good estimate of the adequacy of preload. At this point, the anesthesiologist and surgeon jointly determine whether myocardial filling and performance are adequate. This determination can best be accomplished by using TEE to observe the global and regional function of both ventricles. Supplemental information can be obtained by measuring CO, if possible. Afterload can also be optimized at this point. Usually, 95 to 125 mm Hg is a desirable systolic pressure in adult patients in the immediate postbypass period, whereas increased systolic

blood pressure should be avoided to prevent excessive stress on suture lines in the heart and aorta. If the patient is hemodynamically unstable and additional time is needed to administer initial or additional inotropes or vasoconstrictors, CPB can be reinstated by unclamping the venous outflow line and directing all flow to the oxygenator again (Fig. 54.11).

Once protamine is administered, the reinstitution of CPB becomes a more complicated process because the patient must first be reheparinized and antithrombin levels may be inadequate. Therefore, final checks of cardiac function, heart rate and rhythm, preload, afterload, and perfusion should be made jointly by the anesthesiologist and the surgeon. The venous cannula or cannulas are usually removed after the initial test dose of protamine is given. Many surgeons remove the aortic cannula only after at least half of the protamine dose has been administered. The rate and mode of protamine administration (incremental small boluses vs. continuous infusion) vary according to institutional and individual clinicians' practices, but a large dose of protamine should never be administered as a rapid bolus.

Table 54.5 shows the characteristics and treatment modalities of specific TEE-diagnosed difficulties that may be encountered during weaning and termination from CPB.¹⁴⁷

CHEST CLOSURE

As the cardiac surgery proceeds toward its conclusion a critical step is still to come—chest closure. Chest closure is important because of the hemodynamic consequences that can result from it.

Usually the surgical team would announce the closure of the chest to the anesthesia team, but the anesthesiologists should remain vigilant of the timing of chest closure even if the surgeons do not announce it.

In the immediate post-CPB period patients are generally hypovolemic. Closure of the chest would exacerbate the consequence of hypovolemia (i.e., hypotension). To prepare for chest closure, anesthesiologists administer crystalloid, colloid, or blood depending on the patient's requirement. If chest closure causes severe hypotension surgeons should be requested to reopen the chest and wait until volume resuscitation has caught up (or at least the volume status is relatively easily manageable) to close the chest.

In addition to hypovolemia, chest closure is important in regard to causing ischemic changes by impinging on a venous or arterial graft that lies in a vulnerable position on or around the heart. In this situation ECG and/or hemodynamic changes will be observed which should prompt the anesthesiologist to inform the surgical team, who will reopen the chest and reposition the graft in a way that it is not affected by chest closure.

Other reasons for severe hypotension during chest closure in addition to hypovolemia and ischemia secondary to kinking of a coronary graft include impairment of RV contractility and venous return in patients with significant myocardial edema. TEE can be particularly useful in determining the cause of hypotension during chest closure because it can quickly reveal tamponade, hypovolemia, RV or LV global dysfunction, and severe new

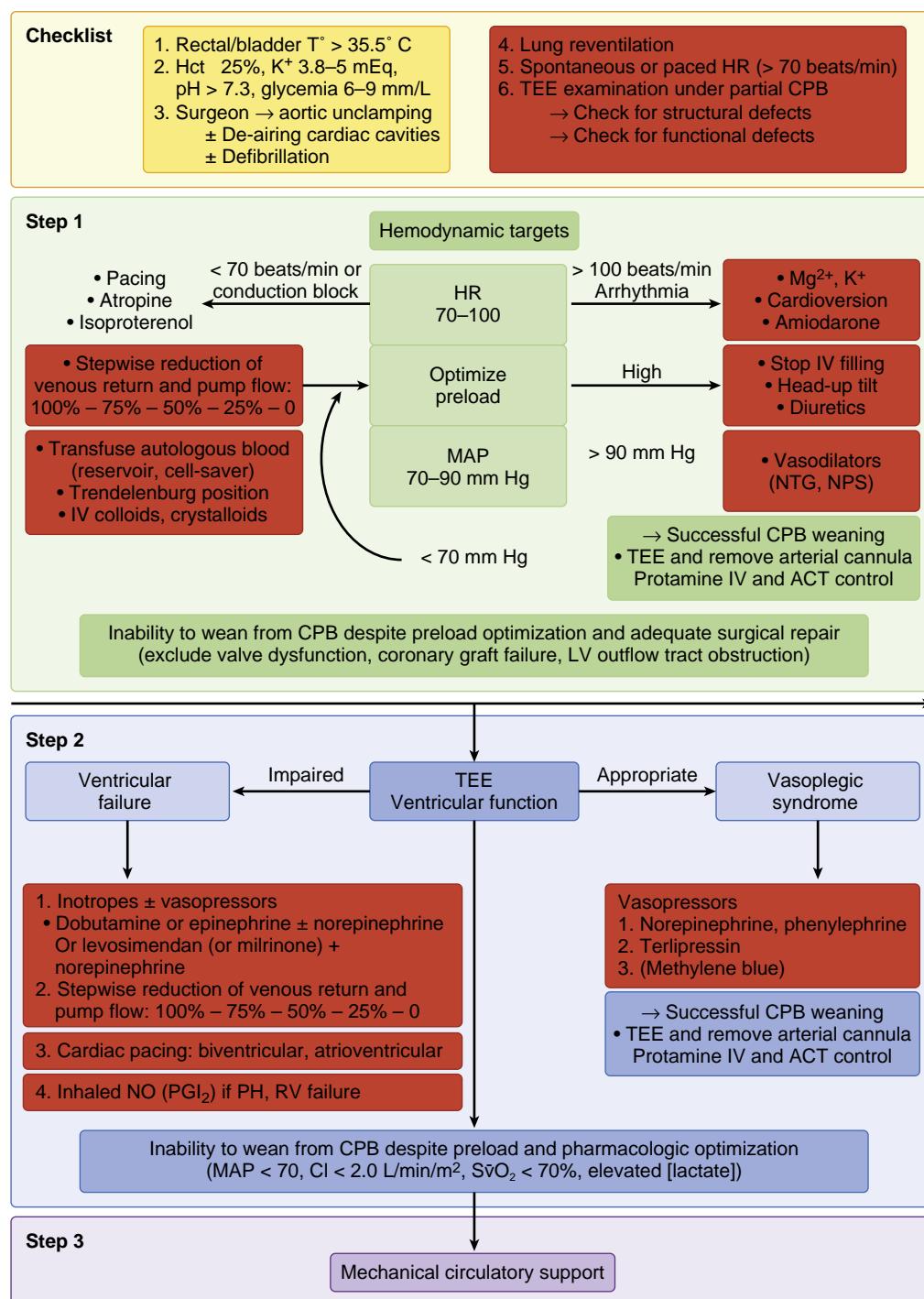


Fig. 54.11 Algorithm for weaning from cardiopulmonary bypass (CPB). ACT, Activated clotting time; Hct, hematocrit; HR, heart rate; IV, intravenous; K^+ , potassium; LV, left ventricular; MAP, mean arterial pressure; Mg^{2+} , magnesium; NO, nitric oxide; NPS, sodium nitroprusside; NTG, nitroglycerin; PGI_2 , prostacyclin; PH, pulmonary hypertension; RV, right ventricular; SvO_2 , mixed venous oxygen saturation; TEE, transesophageal echocardiography. (From Licker M, Diaper J, Cartier V, et al. Clinical review: management of weaning from cardiopulmonary bypass. *Ann Card Anaesth*. 2012;15:206–223.)

wall motion abnormalities. Reopening the chest may be necessary while treatment is instituted. Occasionally, the patient's sternum cannot be closed because of hemodynamic instability; in such cases, only skin closure is attempted, and plans are made to return to the operating room for sternal wiring after a period of myocardial recovery in the ICU.

TRANSPORT TO THE INTENSIVE CARE UNIT

Transportation of postcardiac surgical patients to the ICU is frequently dangerous and underestimated. Preparation for transportation of a postcardiac surgical patient should start with evaluation of the stability of the patient in the operating room. An ICU bed with a portable

TABLE 54.5 Characteristics and Treatment Modalities of Weaning Difficulties

Surgical or Technical Failure		Ventricular Dysfunction	Vasoplegic Syndrome	Left Ventricular Outflow Tract Obstruction
Diagnostic criteria	TEE Valvular regurgitation or stenosis Patient-prosthesis mismatch Paraprosthetic leakage Intracardiac shunt Occluded vascular graft	1. TEE ↓ Contractility of LV and RV Dilated LV and RV ↓ Relaxation 2. Hemodynamics ↓ CO and ↓ MAP	1. TEE Preserved ventricular contractility 2. Hemodynamics ↑ Or normal CO and ↓ MAP	TEE Systolic anterior motion of anterior mitral leaflet LV septal hypertrophy Pressure gradient in LV outflow tract
Incidence	2%-6%	15%-40%	4%-20%	5%-10% after mitral valve surgery
Risk factors	Team and operator's experience, qualification Low surgical volume Extended disease, difficult anatomy	Age (>65 years), female sex CHF, low LVEF LV diastolic dysfunction Previous MI, COPD eGFR < 60 mL/min Extensive CAD, left main CAD Reoperation, emergency, combined procedure Prolonged CPB	Preoperative therapy with ACEI or angiotensin II antagonist, β -blockers, heparin High EuroScore Prolonged CPB Low LVEF (<35%)	Myxomatous mitral valve Hyperdynamic LV Short distance between MV coaptation point and LV septum
Specific treatment	Reoperation Secondary repair or valve replacement Shunt closure Additional coronary bypass graft	1. Drugs Adrenergic agonists (dobutamine, epinephrine, dopamine) Phosphodiesterase inhibitors (milrinone) Calcium sensitizer (levosimendan) Systemic vasodilators (NTG, NPS) Pulmonary vasodilators (NO, PGI_2) 2. Electromechanical Support Biventricular pacing Intraaortic balloon pump Extracorporeal membrane oxygenation Ventricular assist device	Vasopressors Phenylephrine Norepinephrine Terlipressin Methylene blue	1. Medical Volume expansion Inotrope discontinuation β -blockers 2. Surgical Septal bulge resection MV repeat repair or replacement

ACEI, Angiotensin-converting enzyme inhibitor; CAD, coronary artery disease; CHF, congestive heart failure; CO, cardiac output; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; eGFR, estimated glomerular filtration rate; LV, left ventricle; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; MI, myocardial infarction; MV, mitral valve; NO, nitric oxide; NPS, nitroprusside sodium; NTG, nitroglycerin; PGI_2 , prostacyclin; RV, right ventricle; TEE, transesophageal echocardiography.

From Licker M, Diaper J, Cartier V, et al. Clinical review: management of weaning from cardiopulmonary bypass. *Ann Card Anaesth*. 2012;15:206-223.

hemodynamic monitor should be prepared and ready for these patients. Monitoring should not be completely interrupted even for a few moments. The ideal transport monitoring system has a “brick” that can be ejected from the operating room monitor and is compatible with the transport monitor. If such equipment is not available, sequential disconnection of monitors is advised so that an online monitor is always visible and the patient is never “unmonitored.”

Staff should be educated about the importance of sequential transfer of monitors.

In the post-CPB period patients are frequently receiving infusions. A cardiac anesthesiologist should make sure that the pumps used for infusions in cardiac surgery are adequately functional. It is a good practice to unplug infusion pumps a few minutes before leaving the operating room to test the battery life for transport. Regardless of the proximity of the ICU to the operating room, disconnection of vasoactive infusions during transport could be devastating in certain critically ill patients.

As many patients are transported intubated, it is a good practice to carry a laryngoscope blade and an endotracheal tube. Even if the patient is extubated before leaving the operating room, airway management equipment and a means

to ventilate the patient should still travel to the ICU with the patient. In addition, emergency medications should be brought during transport. It is recommended that the anesthesiologist carries at least one round of “code drugs” to assist in the event of cardiac arrest during transportation. A defibrillator should be on every patient’s transportation bed.

Upon reaching the ICU, it is the responsibility of the cardiac anesthesiologist to ensure that a detailed report is given to the receiving physician or nurses.

On arrival in the ICU or cardiac recovery area, a transfer of the patient and the patient’s information from one team to another, termed handoff or handover, occurs. Handoff failures have been identified as a significant source of medical errors, both between and within teams.¹⁵⁰⁻¹⁵² Implementing a handoff protocol reduces information omission and reduces errors. The process is intended to be strictly sequential: monitoring should be transferred before ventilator transfer, and all phase 1 items should be completed before information transfer.^{153,154} Using formal, sequential handoff procedures does not increase the duration of the process.¹⁵⁵ The following sequence is suggested¹⁵⁵ (Wahr J, personal communication, November 17, 2012):

Phase 1: Equipment and Technology Handover

1. Monitoring transferred to ICU equipment
2. Ventilator function initiated
3. Infusions and fluids checked
4. Chest drains secured and on suction
5. Vital signs confirmed to be stable, ventilator functioning well, infusions running appropriately
6. Anesthesiologist, nurse, and surgeon confirm that they are ready for information transfer

Phase 2: Information Handover

1. Anesthesiologist presents
 - a. Patient-specific information (age, weight, medical and surgical history, allergy status, baseline vital signs, pertinent laboratory results, diagnosis, current condition, and vital signs)
 - b. Anesthetic information (intraoperative course and any complications, lines present, blood transfusion or fluid totals, paralytics or opioids, antibiotics, current infusions, vital sign parameters or limits, pain relief plan, laboratory values)
2. Surgeon presents: surgical course (diagnosis, operation performed, surgical findings, complications, blood loss, drains, antibiotic plan, deep vein thrombosis prophylaxis, medication plan, tests to be done, nutrition, key goals for the next 6 to 12 hours)

Phase 3: Questions and Discussion

In all cases, the anesthesiologist should remain with the patient until hemodynamic stability and overall stability are ensured.

THE POSTBYPASS PERIOD: COMMON PROBLEMS AFTER CARDIOPULMONARY BYPASS

Awareness

The potential for the patient's awareness must be assessed during and after CPB (see also [Chapter 40](#)). The incidence of this distressing complication is more frequent in cardiac operations than in other cases.^{156,157} Although patients may sweat during the rewarming period, usually because of perfusion of the thermoregulatory site in the hypothalamus with warm blood, sweating may also result from awareness if anesthetic concentrations are low during the period when the brain becomes normothermic. Awareness may be more likely if considerable time has elapsed since any sedative-hypnotic or narcotic has been administered, if small doses of anesthetic drugs were administered during CPB, or if the patient is young. Consideration should be given to continuing to administer a volatile anesthetic agent once pulmonary ventilation is reestablished and to administering additional sedative-hypnotic doses, an opioid, or both. Some clinicians begin infusing an anesthetic agent such as propofol or dexmedetomidine shortly after weaning the patient from CPB and continue it during and after transport to the ICU or cardiac recovery area.

Published studies support the hypothesis that the use of depth-of-anesthesia monitors such as the BIS can decrease the incidence of intraoperative awareness in patients at high risk for this problem (see also [Chapter 40](#)).^{156,157} However, falsely high BIS values during cardiac surgery

BOX 54.8 Risk Factors for Low Cardiac Output Syndrome After Cardiopulmonary Bypass

- Preoperative left ventricular dysfunction
- Valvular heart disease requiring repair or replacement
- Long aortic cross-clamp time and total cardiopulmonary bypass time
- Inadequate cardiac surgical repair
- Myocardial ischemia and reperfusion
- Residual effects of cardioplegia solution
- Poor myocardial preservation
- Reperfusion injury and inflammatory changes

From Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:1028.

have been attributed to interference from pump head rotation, pacemakers, and hypothermia itself.¹⁵⁸ Furthermore, because processing of the raw EEG and data smoothing to generate the BIS number occur over 15 to 30 seconds, the BIS number lags slightly behind clinical events.

Another important decision to be made is whether additional neuromuscular blocking drugs are needed during and after weaning from CPB. Use of a peripheral nerve stimulator may facilitate this decision (see also [Chapter 43](#)). Although movement of the patient may serve as an indication of the patient's awareness, such movement can be extremely dangerous if it results in dislodgment of the aortic or venous cannulas. Furthermore, shivering can occur because of the "afterdrop" in temperature after a period of hypothermic CPB. Because shivering can increase oxygen demand by 300% to 600%, it should be prevented by administering a neuromuscular blocking drug.

Cardiovascular Decompensation (Low Cardiac Output Syndrome)

Although improvements in myocardial protection have occurred during recent decades, it is well documented that significant declines in LV function after CABG and other cardiac operations occur in the first 8 to 24 postoperative hours.¹⁵⁹ A combination of ischemia and reperfusion injury after cardiac surgery contributes to an energy deficit state in the myocardium that limits uptake of exogenous energy substrates from blood (Box 54.8). Prolonged aortic cross-clamp time, incomplete revascularization, or poor myocardial preservation adds additional risk. In particular, patients with preexisting LV dysfunction experience a delay in myocardial recovery after cardiac surgery and require measures to relieve the workload of the heart. Furthermore, preexisting diastolic dysfunction is associated with an increased risk of difficulty in weaning from CPB and ongoing need for vasoactive support during the postbypass period and in the ICU.¹⁶⁰

Criteria used to define low CO syndrome (LCOS) include a cardiac index of less than 2.4 L/min/m², elevated lactate levels, and urine output of less than 0.5 mL/h for more than 1 hour.¹⁶¹

Postoperative management of patients at high risk for LCOS requires a physiologic approach. Optimizing preload and reducing afterload help maximize cardiac function.

TABLE 54.6 Relative Potency of Commonly Used Vasoactive Drugs

	Dose	CARDIAC			PERIPHERAL VASCULATURE	
		Heart Rate	Contractility	Vasoconstriction	Vasodilation	Dopaminergic
Norepinephrine	2-40 µg/min	+	++	++++	0	0
Dopamine	1-4 µg/kg/min	+	+	0	+	++++
	4-20 µg/kg/min	++	++, +++, +	++, +++, +	0	++
Epinephrine	1-20 µg/min	++++	++++	++++	+++	0
Phenylephrine	20-200 µg/min	0	0	+++	0	0
Vasopressin	0.01-0.03 units/min	0	0	++++	0	0
Dobutamine	2-20 µg/kg/min	++	++, +++, +	0	++	0
Milrinone	0.375-0.75 µg/kg/min	+	+++	0	++	0
Levosimendan	0.05-0.2 µg/kg/min	+	+++	0	++	0

From Hollenberg SM, Parrillo JE. Acute heart failure and shock. In: Crawford MH, DeMarco J, Paulus WJ, eds. *Cardiology*. 3rd ed. Philadelphia: Saunders; 2010:964.

Both tachycardia and bradycardia should be avoided, and postoperative arrhythmias should be treated. In addition, shivering should be prevented because it raises the heart rate by increasing oxygen demand. Postoperative deep sedation and muscle relaxation are often used to reduce myocardial workload by reducing the body's overall metabolic demand by 25% to 30%.

Pharmacologic support is often needed to improve contractility as the patient is weaned from CPB and, eventually, recovering in the ICU (Table 54.6).^{161,162} Catecholamines (β -adrenergic agonists) and phosphodiesterase inhibitors are the main classes of pharmacologic agents used for this purpose. Catecholamines (e.g., epinephrine, norepinephrine, dopamine, dobutamine, dopexamine, isoproterenol) are often the first line of therapy. They exert positive inotropic action by stimulating the β_1 receptor, which leads to increased intracellular cyclic adenosine monophosphate (cAMP). The predominant hemodynamic effect of a specific catecholamine depends upon the degree to which the α , β_1 , β_2 , and dopaminergic receptors are stimulated. Phosphodiesterase inhibitors (e.g., milrinone, amrinone), sometimes termed inodilators, may be used either as first-line therapy or added to β -adrenergic therapy. Phosphodiesterase inhibitors augment β -adrenergic stimulation by inhibiting the breakdown of cAMP. When these drugs are added to catecholamine infusions, the result is an additive or possibly synergistic increase in inotropy. Phosphodiesterase inhibitors also induce systemic and pulmonary vasodilation. Hence, they are particularly useful in patients with pulmonary hypertension, RV failure, or aortic or mitral valve regurgitation.

Although not yet available in the United States, a newer class of drugs—the calcium sensitizers—exhibit potent inodilatory properties.^{163,164} Levosimendan is the first such drug in this class, and has been studied extensively in other parts of the world. A randomized controlled trial of levosimendan in cardiac surgery in the U.S., (although it was found to be beneficial), did not meet its primary endpoint,¹⁶⁵ and thus the drug has not received approval by the U.S. FDA. Its mechanism of action is that it increases myocyte sensitivity to calcium by stabilization of the calcium binding to troponin C, thus enhancing actin-myosin

cross-bridging and increasing contractility.¹⁶⁶ Therefore, inotropic performance is enhanced, whereas diastolic performance is preserved. Like phosphodiesterase inhibitors, levosimendan may augment inotropy without significantly increasing myocardial oxygen consumption.

RV failure may also be present in patients with LCOS, and it manifests as elevated PA and CVP pressures. Echocardiography can be diagnostic—findings include an enlarged and poorly contracting right ventricle, often with significant TR. The management of RV failure consists of ensuring adequate RV filling and maintaining adequate systemic pressures to prevent RV ischemia. Afterload reduction with agents effective in the pulmonary circulation is helpful. Milrinone may reduce PVR and improve CO. Nitric oxide and inhaled prostaglandins are selective for pulmonary vasodilation. Other measures to decrease PVR include hyperventilation (higher respiratory rate) to induce mild hypocapnia and aggressive treatment of hypoxemia and acidosis.

Right Heart Failure

Any situation where the right heart is not able to fulfill the requirements of circulation is labelled as right HF. With the development of new imaging modalities, it has become easy to accurately evaluate the right heart for management purposes.

Box 54.9 lists the key points of right HF which include the importance of identifying the problem in a timely manner with the help of new imaging modalities. A cardiac anesthesiologist can play a key role in this regard by using the three-dimensional TEE imaging. A number of parameters are used to evaluate right HF by the cardiac anesthesiologist using TEE: size of the right atrium and ventricle, RV systolic function, septal curvature, tricuspid regurgitation (TR), gradient across the RV outflow tract, and an estimation of the PA and RA pressures.¹⁶⁷

Management of right HF starts by identifying the etiology of failure: ischemia, PE, outflow tract obstruction, air embolism, etc. Maintenance of sinus rhythm, reducing RV afterload, and inotropic support play an important role in supporting the right heart. Importance of maintaining adequate MAP should not be underestimated in these cases.

BOX 54.9 Key Points of Right Heart Failure

- Right ventricular (RV) function is associated with significant mortality
- New echocardiographic modalities using strain appear promising in predicting RV failure
- Monitoring the impact of RV function using near infrared spectroscopy and liver hemodynamics appear as useful intraoperative methods in adjusting therapeutic interventions and fluid management

From Haddad F, Elmi-Sarabi M, Fadel E, et al. Pearls and pitfalls in managing right heart failure in cardiac surgery. *Curr Opin Anesthesiol*. 2016;29:68–79.

Inhaled vasodilators are also used in right HF. In some institutions two inhaled agents are instituted with different mechanisms of action, especially in unexpected right HF cases.

Fluid management in these patients should be very judicious as they might already be congested.

Finally, mechanical support for the failing right heart is available and has seen significant advancement in the last few years. Depending on the situation of the patient, these devices can be either temporary or permanent in nature.¹⁶⁷

Right Ventricular Dysfunction or Failure

RV dysfunction or failure may also occur after CPB, usually because of inadequate myocardial protection, inadequate revascularization with resultant RV ischemia or infarction, preexisting pulmonary hypertension, intracoronary or pulmonary air embolism, chronic mitral valve disease, or TR. Such RV failure may be evidenced by RV distention and hypokinesis on TEE, as well as by elevations in CVP and PA pressure (PAP).

Therapy for RV failure includes increasing preload and inotropic support; milrinone, dobutamine, and isoproterenol are the usual first-line drugs. Other pharmacologic drugs occasionally used to induce pulmonary vasodilation include nitroglycerin and nitroprusside. One potential problem with the use of intravenous inodilator and vasodilator agents is that their effects are not limited to the pulmonary circulation. SVR must be adequate to maintain RV perfusion pressure. Inhaled drugs such as nitric oxide, epoprostenol (Flolan), and inhaled iloprost are considered in refractory cases. Adjuncts to decrease PVR include hyperventilation (higher respiratory rate) to induce mild hypocapnia, and preventing hypoxemia and acidosis. Rarely, patients may require support with an RVAD.

Vasoplegia

Inappropriate vasodilation with a low SVR is another common cause of immediate post-CPB cardiovascular decompensation that may result in unacceptable hypotension. Predisposing factors include long-term administration of medications such as ACEIs or angiotensin receptor blockers (ARBs), prolonged duration of CPB, severe anemia with decreased viscosity, acid-base disturbances, and sepsis. Treatment with infusion of a vasoconstrictor drug such as phenylephrine, norepinephrine, vasopressin, or, rarely, methylene blue or B12 is usually successful.

TABLE 54.7 Postoperative Rate and Rhythm Disturbances

Disturbance	Usual Causes	Treatments
Sinus bradycardia	Preoperative or intraoperative β blockade	Atrial pacing β -Agonist Anticholinergic
Heart block (first, second, and third degree)	Ischemia Surgical trauma	Atrioventricular sequential pacing Catecholamines
Sinus tachycardia	Agitation or pain Hypovolemia Catecholamines	Sedation or analgesia Volume administration Change or stopping of drug
Atrial tachyarrhythmias	Catecholamines Chamber distention Electrolyte disorder (hypokalemia, hypomagnesemia)	Change or stopping of drug Treatment of underlying cause (e.g., vasodilator, give K^+ / Mg^{2+}) Possible need for synchronized cardioversion or pharmacotherapy
Ventricular tachycardia or fibrillation	Ischemia Catecholamines	Cardioversion Treatment of ischemia; possible need for pharmacotherapy Change or stopping of drug

K^+ , Potassium; Mg^{2+} , magnesium.

Modified from Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:1030.

Dysrhythmias

Normal sinus rhythm is ideal because it provides an atrial contribution to ventricular filling and a normal synchronized contraction of the ventricle. However, either supraventricular or ventricular arrhythmias can occur in the immediate postbypass period.

Postoperative arrhythmias are frequently seen in postcardiac surgical procedures. Table 54.7¹⁶⁸ summarizes causes and treatments of common postoperative arrhythmias. Postoperative arrhythmias can be divided into atrial and ventricular arrhythmias.

Atrial Arrhythmias. Atrial fibrillation (AF) is the most common postoperative arrhythmia (27%–40%).^{169,170} Patients are at highest risk for new-onset atrial fibrillation 2 to 3 days after cardiac surgery.¹⁷⁰ This arrhythmia can potentially prolong the patient's hospital stay and increase management costs by causing hemodynamic compromise or thromboembolic complications in the postoperative period.¹⁷¹

Many potential risk factors have been studied in efforts to predict the occurrence of postoperative atrial fibrillation. With advancing age, dilatation of the atrium interrupts cell-to-cell electrical coupling between atrial muscle fibers. Other preoperative risk factors for postoperative atrial fibrillation include a history of atrial fibrillation, chronic obstructive pulmonary disease, valve surgery, and postoperative withdrawal of a β -blocker or ACEI.¹⁷⁰

Increased preoperative hemoglobin A1c,¹⁷² physical activity of low intensity during 1 year prior to surgery,¹⁷³ Caucasian race,¹⁷⁴ obesity, and electrolyte disturbances (hypokalemia, hypomagnesemia) have also been shown to contribute towards increased risk of atrial fibrillation.

Perioperative factors include inadequate atrial protection during surgery, pericardial inflammation, autonomic imbalance during the postoperative period, change in atrial size with fluid shifts, electrolyte (potassium and magnesium) abnormalities, and excessive production of catecholamines.¹⁷⁵ Reduced risk has been associated with the postoperative administration of β -blockers, ACEIs, potassium supplementation, and nonsteroidal antiinflammatory drugs (NSAIDs).¹⁷⁰

Treatment for atrial fibrillation includes both pharmacologic agents and electrical stimulation. Many studies have shown that β blockade significantly reduces the incidence of postoperative atrial fibrillation and that withdrawal of β -blockers increases risk.^{176,177} Synchronized cardioversion is reserved for patients who show signs of hemodynamic instability during atrial fibrillation.¹⁷⁸ In the absence of hemodynamic instability, pharmacologic agents are used with the goal of preventing a rapid ventricular response. Drugs usually employed for this purpose include calcium channel blockers, β -blockers, magnesium, and amiodarone. Expert consultation should be obtained before treatment is initiated, especially in a stable patient.^{177,178}

Ventricular Arrhythmias. Although ventricular arrhythmias occur after cardiac surgical procedures, sustained ventricular arrhythmias are relatively uncommon. Associated factors may include hemodynamic instability, electrolyte abnormalities, hypoxia, hypovolemia, ischemia or infarction, acute graft closure reperfusion, and the use of inotropic agents.¹⁷⁸

Ventricular arrhythmias can range from simple premature ventricular complexes (PVCs) to VT. Simple PVCs do not pose a significant risk of life-threatening ventricular arrhythmia. Conversely, complex ventricular arrhythmias, including both frequent PVCs ($>30/h$) and nonsustained VT, may make patients prone to sudden death, especially in the long term. Sudden death is even more likely if ventricular function is also compromised. A study of 126 patients with postoperative complex ventricular ectopy found a mortality rate of 75%.¹⁷⁸ Patients with sustained ventricular arrhythmias have a poor prognosis in both the short and the long term.

Although hemodynamically unstable VT should be treated by synchronized cardioversion, patients with PVCs or short runs of nonsustained VT with hemodynamic stability do not need to be treated. Any reversible causes should be sought and corrected. Amiodarone is reserved for hemodynamically stable patients with VT or an uncertain rhythm. Ventricular fibrillation should be treated promptly with electrical defibrillation.¹⁷⁸ For long-term management of ventricular arrhythmias, in addition to antiarrhythmic agents, electrophysiologic studies or placement of an ICD should be considered.

Bradyarrhythmias. Bradyarrhythmias are not uncommon in the immediate postoperative period. In most cases, a temporary epicardial pacemaker is sufficient. In

BOX 54.10 Vasodilators Available for the Treatment of Perioperative Hypertension

Adenosine
 α_1 -Adrenergic antagonists
 α_2 -Adrenergic agonists
 Angiotensin-converting enzyme inhibitors (enalaprilat)
 Angiotensin II antagonists
 Atrial natriuretic peptide (nesiritide)
 β_2 -Adrenergic agonists
 Dihydropyridine-type calcium channel blockers*
 Dopamine agonists
 Hydralazine
 Nitrovasodilators*
 Phosphodiesterase enzyme inhibitors
 Prostaglandins

*Intravenous vasoactive therapies in widespread use to treat perioperative hypertension.

From Levy JH. Management of systemic and pulmonary hypertension. *Tex Heart Inst J*. 2005;32:467–471.

a small percentage of patients, a permanent pacemaker may be necessary, especially in patients with sinus node dysfunction or AV conduction disturbances after either CABG or valve repair.¹⁷⁸ Patients who need a permanent pacemaker may receive either a single-chamber or a dual-chamber pacemaker. Multiple factors dictate which particular device would most benefit an individual patient.¹⁷⁹

Hypertension

Immediately after cardiac surgery, the patient remains prone to hemodynamic instability, including hypertension.¹⁸⁰ Causes of postoperative hypertension are often multifactorial and may include withdrawal from preoperative antihypertensive medications (e.g., β -blockers and centrally acting α_2 -agonists), pain, hypoxemia, hypercarbia, and hypothermia. However, arterial vasoconstriction usually plays a central role in acute postoperative hypertension.¹⁸¹ The hazards of untreated postoperative hypertension include increased myocardial work and oxygen consumption, MI, rhythm disturbances, cerebrovascular accidents, increased bleeding, and even suture line disruption. In the postoperative period, deepening sedation to control a hypertensive episode may not be the best or the only possible approach, particularly if early extubation (fast tracking) is desirable.^{180,181}

Several pharmacologic agents are available for use as antihypertensive agents (Box 54.10).¹⁸¹ The drugs most commonly used in clinical practice are the nitrovasodilators and the dihydropyridine-type calcium channel blockers. Because of its antiischemic effects and familiarity, nitroglycerin is often the first agent used to treat hypertension in patients who have undergone coronary revascularization. However, nitroglycerin is not always effective in such patients because it primarily causes venodilation rather than arterial dilation. In addition, patients tend to develop tolerance to nitroglycerin.¹⁸¹

Because arterial vasoconstriction plays an important role in the development of hypertension after cardiac surgery, the therapeutic agent chosen should usually be one that effectively reduces this vasoconstriction. Sodium

nitroprusside, a nonspecific venous and arterial vasodilator, is a common choice. Though the risks of coronary steal with nitroprusside are theoretical,¹⁸¹ patients with renal failure eliminate sodium nitroprusside more slowly than normal, which makes them vulnerable to the toxic effects of this drug's metabolites (cyanide and thiocyanate).

Fenoldopam is a short-acting dopamine agonist that causes arterial-specific vasodilation by stimulating D₁-receptors. Unlike sodium nitroprusside, fenoldopam increases renal blood flow to produce diuresis and natriuresis.¹⁸² Nevertheless, the results of most clinical trials regarding the renal protective effects of fenoldopam are equivocal. In addition, severe hypertension may require higher doses of fenoldopam, which may be associated with undesirable increases in heart rate.

Dihydropyridine-type calcium channel blockers, such as nicardipine and clevipipine, selectively relax arterial resistance vessels without negative inotropic or dromotropic (conduction) effects and cause generalized vasodilation of the renal, cerebral, intestinal, and coronary vascular beds. Recently, due to manufacturing issues with nitroprusside, the price in the U.S. has risen to several thousands of dollars. For this reason, the author's institution now uses nicardipine as a first-line drug to treat hypertension.

It is important to ensure that the patient's intraarterial pressure is monitored adequately when any vasoactive agent is administered. Vasoconstriction or poor perfusion of the extremities may create a discrepancy between central aortic and peripheral arterial pressures.

While monitoring a patient's blood pressure it is important to take note of the position of the arterial line transducer. A transducer placed lower than the mid axillary line will give artificially high blood pressure readings. In addition, a short radial arterial catheter may be "positional" if hand positioning is suboptimal, or "dampening" of the tracing may result from poor perfusion of the distal extremities. Occasionally, during the perioperative period, the cardiac anesthesiologist or surgeon must replace a distal peripheral arterial catheter (e.g., with a femoral arterial catheter) to ensure that the effects of vasoactive therapy are monitored accurately.

Renal Insufficiency

Perioperative renal failure that necessitates dialysis occurs in approximately 2% of patients.¹⁸³ Although the definition of renal insufficiency or failure varies among studies, three useful criteria are (1) a serum creatinine level more than 44 mmol/L (>0.5 mg/dL) higher than its preoperative value, (2) a serum creatinine level more than 50% greater than its preoperative value, and (3) a serum creatinine level more than 177 mmol/L (>2.0 mg/dL).¹⁸⁴ Another definition of acute renal insufficiency involves a classification scheme that uses the acronym RIFLE (Table 54.8).¹⁸⁵

Preoperative risk factors that are commonly associated with postoperative renal dysfunction after cardiac operations include preexisting renal insufficiency, type 1 diabetes mellitus, age older than 65 years, major vascular surgery, arteriopathy, genetic predisposition, and recent exposure to nephrotoxic agents (e.g., radiocontrast dyes, bile pigments, aminoglycoside antibiotics, and NSAIDs).^{183,184} Ejaz and colleagues showed that in addition to serum creatinine, serum uric acid is a significant predictor of AKI.¹⁸⁶

TABLE 54.8 RIFLE* Classification Scheme for Acute Renal Failure

	GFR Criteria	Urine Output Criteria
Risk	Plasma creatinine increased $1.5\times$ or GFR decrease $>25\%$	<0.5 mL/kg/h $\times 6$ h
Injury	Plasma creatinine increased $2\times$ or GFR decrease $>50\%$	<0.5 mL/kg/h $\times 12$ h
Failure	Plasma creatinine increased $3\times$, acute plasma creatinine ≥ 350 μ mol/L, or acute rise ≥ 44 μ mol/L	<0.3 mL/kg/h $\times 24$ h or anuria $\times 12$ h
Loss	Persistent acute renal failure = complete loss of kidney function >4 weeks	
ESKD	End-stage kidney disease (>3 months)	

*Acronym for risk, injury, failure, loss, and end-stage kidney disease.
ESKD, End-stage kidney disease; GFR, glomerular filtration rate.

From Kuitunen A, Vento A, Suojaranta-Ylinen R, et al. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg*. 2006;81:542–546.

In addition, several intraoperative factors may predispose a patient to renal dysfunction, including the need for emergency surgery, repeat cardiac surgery, valve surgery, and a CPB time exceeding 3 hours.^{183,184} Other perioperative risk factors for renal dysfunction after cardiac surgery are hypovolemia, hypotension resulting from either hypovolemia or LCOS, and embolic phenomena. Furthermore, damage to nephrons in the medullary region of the kidney results in acute tubular necrosis; hypoxia is a common cause of damage to the nephrons in this region.¹⁸⁴

Postoperative renal insufficiency in cardiac surgical patients is associated with longer ICU stay, longer overall hospital stay, and increased mortality.^{183,184} Thus, this disorder should be prevented whenever possible. On the basis of studies conducted in patients with radiocontrast nephropathies, investigators theorized that hydration before radiocontrast media are administered may protect the kidneys.¹⁸⁴ Because the mechanism of renal injury after CPB appears similar to that triggered by the administration of radiocontrast dyes, it is thought that adequate hydration and maintaining normovolemia can help to prevent postoperative renal dysfunction in cardiac surgical patients.¹⁸⁴

Several treatment modalities have been suggested to prevent or ameliorate postoperative renal dysfunction (Box 54.11).¹⁸⁴ Basic supportive therapy involves ensuring adequate CO, perfusion pressure, and intravascular volume. Discontinuing any nephrotoxic drug (NSAIDs, certain antibiotics) is usual. Diuretics are not helpful and may be harmful.¹⁸⁷ Unproven pharmacologic therapies include mannitol, calcium channel blockers, ACEIs, atrial natriuretic peptide, and N-acetylcysteine. Finally, if dialysis is needed, continuous dialysis may be better than intermittent dialysis.¹⁸⁸

Central Nervous System Dysfunction

The risk of overt postoperative stroke has decreased over the last few decades.³⁰ However, an increased risk of neurologic complications remains in older patients,¹⁸⁹ as well as in patients undergoing combined CABG and valvular heart

BOX 54.11 Aims of and Treatment Modalities to Reduce or Prevent the Development of Postoperative Renal Dysfunction

1. Maintain adequate oxygen delivery—by ensuring adequate cardiac output, adequate oxygen-carrying capacity, and proper hemoglobin saturation.
2. Suppress renovascular constriction—by ensuring adequate volume preload and use of infusions of mannitol, calcium entry blockers, and angiotensin-converting enzyme inhibitors.
3. Promote renal vasodilation—by dopaminergic agents, prostaglandins, and atrial natriuretic peptide.
4. Maintain renal tubular flow—by loop diuretics and mannitol (which may act to prevent tubular obstruction, which can cause cellular swelling, ischemia, and death).
5. Decrease oxygen demand—by the use of loop diuretics and mild cooling.
6. Attenuate ischemic reperfusion injury—as a result of the release of oxygen free radicals and calcium ions.

Modified from Sear JW. Kidney dysfunction in the postoperative period.

Br J Anaesth. 2005;95:20–32.

surgery or other complex cardiac surgical procedures.¹⁹⁰ Risk factors for overt neurologic complications are listed in **Box 54.4**. The impact of overt stroke is profound in terms of worse adjusted hospital outcomes, longer ICU and postoperative stays, and poorer downstream survival.¹⁹¹

A less well-defined entity, POCD or the newer terminology of PND, is far more common. Delirium is included in the definition of POCD, as are deficits of memory, concentration, and psychomotor speed. Early cognitive loss, once thought to be transient, may persist for 5 years after cardiac surgery in as many as 40% of patients.¹⁹² Formerly, POCD was assumed to be caused by physiologic disturbances resulting from CPB. However, more recent studies have confirmed that POCD occurs with similar frequencies after on-pump cardiac surgery, off-pump cardiac surgery, coronary stenting, and noncardiac surgery.¹⁹³ Hence, current attention focuses on factors related to surgical stress, anesthetic agents, and patient-related predisposing factors, particularly the degree of preoperative cerebrovascular disease.^{194,195} In fact, surgical procedures are likely to uncover a patient's susceptibility to cognitive loss that was already present and would eventually manifest even without surgery, usually as a result of the progression of cerebrovascular disease.¹⁹⁵ Although POCD is less devastating than stroke, its potential impact on quality of life and overall healthcare resource use is still profound.¹⁹⁶

Neuroprotection Strategies. Numerous strategies have been tried to decrease the incidence and severity of neurologic injury in cardiac surgical patients. The most common nonpharmacologic approaches emphasize the reduction of macroemboli and microemboli. As described in earlier sections of this chapter, these strategies include avoiding aortic atheroma by using transesophageal or epiaortic echocardiography, optimizing the placement of the aortic cannula in the aorta, avoiding partial occlusion clamping of the aorta for proximal anastomoses by using a single cross-clamp, and, in selected patients, avoiding all cross-clamping of the

aorta (the “no touch technique”).^{43,197,198} Other strategies to minimize particulate microemboli include the routine use of arterial filtration in the cardiopulmonary circuit and use of the cell saver before reinfusing blood suctioned into the cardiotomy, to remove particulate and lipid material.¹⁹⁹ Strategies to minimize air microemboli include carefully removing air after any procedure involving opening a cardiac chamber, and flooding the field with carbon dioxide to minimize embolism of air entrained into the heart from the surgical field.²⁰⁰ Eliminating CPB by performing off-pump CABG surgery has been touted as a means to reduce emboli in selected patients, but this approach has not decreased POCD rates at 1 or 5 postoperative years.²⁰¹ Many of the late-occurring strokes are probably caused by atrial fibrillation. Early pharmacologic or electrical correction and adequate anticoagulation are mandatory (see the section on arrhythmias in the postoperative period).

Other nonpharmacologic approaches include perioperative temperature control, as well as blood gas management (α -stat or pH-stat) during hypothermic CPB. These considerations are discussed in the section on CPB.

Diabetes is recognized as a risk factor for stroke and delirium after cardiac operations.²⁰² Even in nondiabetic patients, hyperglycemia is extremely common during cardiac surgical procedures because of the stress response to surgery (as well as CPB), the resultant increases in circulating catecholamines and cortisol, and hypothermia-induced reductions in insulin effectiveness. Experimental evidence has revealed a relationship between hyperglycemia and worse outcome after different types of neurologic injury. However, attenuating the hyperglycemic response to cardiac surgery or CPB has proved difficult. Furthermore, concerns exist regarding inducing even a single episode of severe hypoglycemia with aggressive attempts to control glucose levels.²⁰³ The aim of perioperative glucose control for most patients is a level between 140 and 180 mg/dL.²⁰⁴

The influence of intraoperative hemodynamics may influence neurologic and other outcomes. The prospective, randomized trial conducted by Gold and colleagues compared maintaining “normal” MAP (minimum of 50 mm Hg) with keeping the MAP elevated (target of 80–100 mm Hg).²⁰⁵ These investigators found that the overall incidence of combined cardiac and neurologic complications was significantly lower in the high-MAP group. In another study,²⁰⁶ investigators noted a higher frequency of hypoperfusion-type “watershed” strokes in patients who underwent cardiac surgical procedures with a MAP that was at least 10 mm Hg lower during CPB than before CPB. The current recommendation is to maintain higher targets for MAP (i.e., >50 mm Hg) in patients at high risk for neurologic injury. Because high-risk patients can be identified and a defined therapeutic window exists, pharmacologic protection would be very desirable. However, no definitively proven drug therapy currently exists for the prevention or treatment of neurologic injury after cardiac surgery.

Cerebral oximetry has been proposed to be of benefit in preventing neurologic injury in cardiac surgery, but the evidence is still lacking in this regard.

Postoperative Management of Central Nervous System Injury or Dysfunction. Postoperative stroke may be suggested by the patient's inability to follow commands or

move all extremities shortly after the surgical procedure. Neurologic consultation should be obtained, including diagnostic imaging. Diffusion-weighted magnetic resonance imaging is the most sensitive and accurate imaging technique for postoperative cardiac surgical patients.²⁰⁷ It detects more microembolic lesions than does conventional magnetic resonance imaging and is better able to find multiple watershed lesions.

Management of CNS injury or dysfunction after cardiac operations consists of general supportive measures. Hypotension should be avoided, and consideration should be given to using volume expansion, inotropic augmentation (pharmacologic or mechanical), or vasoactive medications (vasopressin or phenylephrine) to support blood pressure and brain perfusion. The brain oxygen supply-demand balance should be optimized through adequate oxygenation, sedation, and strict temperature control. Hyperthermia (fever) should be aggressively controlled. Both hyperglycemia and hypoglycemia should be avoided. Lytic therapy is of little use in cardiac surgery because it poses a risk of postoperative surgical bleeding.

POCD can manifest subtly, being evident only with psychometric testing, or, at the other extreme, it can manifest as postoperative delirium. *Delirium* is defined as an acute and overt change in cognition and attention, which may include alterations in consciousness and disorganized thinking.²⁰⁸ In the cardiac surgical literature, the reported incidence of delirium depends greatly on the methods used for delirium assessment, varying from 3% (chart review only) to 8% (interviews with nurses); however, with rigorous daily mental status testing and the application of a validated diagnostic algorithm, the incidence may be as high as 53%.²⁰⁹

Risk factors include preexisting cognitive impairment, poor preoperative functional status, prior stroke or transient ischemic attack, depression, alcohol abuse, and abnormal preoperative laboratory values (glucose, sodium, potassium, and albumin).²⁰⁸ Precipitating factors for delirium in the postoperative period include intraoperative and postoperative medications, particularly sedatives and analgesics. The postoperative environment in the ICU often results in sleep deprivation and overstimulation, contributing to the onset of delirium.²⁰⁸ Complications of hospitalization and surgical procedures, including those that result in prolonged controlled ventilation and reduced mobility, also contribute to the development and severity of delirium.

Nonpharmacologic postoperative strategies to prevent delirium are listed in Table 54.9.²⁰⁸ Medications, including those used to control pain and anxiety, are a common cause. Debate continues in the literature for a better drug to minimize the incidence of delirium between benzodiazepines and dexmedetomidine. For patients who develop agitation, the mainstay of treatment is a thorough review of medications, as well as removing other precipitating factors, such as low CO or perfusion state, metabolic disorders (e.g., hyperglycemia), fluid and electrolyte disturbances (hypoglycemia or hyperglycemia and uremia), constipation, urinary retention, and environmental noise. For patients in whom these nonpharmacologic interventions are not sufficient, an antipsychotic, usually haloperidol, is considered first-line therapy for agitation associated with delirium.

TABLE 54.9 Prevention of Delirium after Surgical Procedures

Module	Postoperative Interventions
Cognitive stimulation	Orientation (clock, calendar, orientation board) Avoidance of cognitively active medications
Improvement in sensory input	Glasses Hearing aids and amplifiers
Mobilization	Early mobilization and rehabilitation
Avoidance of psychoactive medication	Elimination of unnecessary medications Pain management protocol
Fluid and nutrition	Fluid management Electrolyte monitoring and repletion Adequate nutrition protocol
Avoidance of hospital complications	Bowel protocol Early removal of urinary catheters Adequate central nervous system oxygen delivery, including supplemental oxygen and transfusion for very low hematocrit Postoperative complication monitoring protocol

Modified from Rudolph JL, Marcantonio ER. Postoperative delirium: acute change with long-term implications. *Anesth Analg*. 2011;112:1202–1211.

Delirium may accelerate cognitive decline in patients with Alzheimer disease or cause a type of posttraumatic stress disorder in younger patients.²⁰⁸ The long-term mental health implications of delirium have not been fully studied but may include impairment of functional recovery.

Peripheral Nerve Injuries. Peripheral nerve injuries are not uncommon in cardiac surgical patients and are often self-limited. These are the result of positioning of the upper extremities with inadequate padding of the ulnar nerve. In addition, the brachial plexus is also prone to injury from excessive stretch by the sternal retractor. Usual presenting symptoms are numbness, weakness, pain, decreased reflexes, and diminished coordination.

Phrenic nerve, recurrent laryngeal nerve, and sympathetic chain injuries have also been reported. Saphenous nerve injury during saphenous vein harvesting is also known to have been reported.

Respiratory Insufficiency

Respiratory failure is a very common complication of cardiac surgery. Pulmonary complications that arise immediately after CPB vary from mild to severe and include atelectasis, bronchospasm, hemothorax, pneumothorax, endobronchial intubation, mucus plugs or blood clots in the endotracheal tube, pulmonary edema, and pulmonary dysfunction that varies from a mild increase in the alveolar-arterial oxygen gradient to a form of adult respiratory distress syndrome (ARDS) known as postperfusion lung syndrome.²¹⁰ Atelectasis is a common cause of decreased arterial oxygenation in the postbypass period because during CPB either the lungs are not ventilated or very small tidal volumes are used. During controlled ventilation, it is common to apply positive end-expiratory pressure after CPB and in the immediate postoperative period.

Hemothorax is caused by the accumulation in the pleural cavity of blood and clot, which should be surgically removed before chest closure. Pneumothorax may result from entry

of the pleural cavity during dissection of the IMA or from excessive positive-pressure ventilation of the lungs. Pneumothorax may not manifest until after chest closure; it is treated by inserting a chest tube. Endobronchial intubation may occur when the patient's head is partially hidden from the anesthesiologist's view. The expansion of both lungs should be confirmed during initial full ventilation before weaning from CPB, when the chest is open, so that a good view of both lungs may be obtained. If any blood or mucus is present in the endotracheal tube, it should be suctioned during and after weaning from CPB.

More severe postoperative respiratory insufficiency that causes difficulty in ventilator weaning may reflect intrinsic pulmonary problems such as CPB-related acute lung injury, transfusion-related acute lung injury, or cardiogenic pulmonary edema. Patients with marginal cardiac function may require diuresis, afterload reduction, or inotropy in order to assist with weaning from mechanical ventilation.

Preoperative efforts to minimize pulmonary complications after cardiac surgery include optimizing pulmonary function for patients undergoing elective surgical procedures.

In previous decades, critical care management after cardiac surgery included overnight mechanical ventilation, which today would be considered "prolonged ventilation." It is clinically important to have a period of controlled ventilation to allow rewarming and emergence from anesthesia, optimize cardiac function, and ensure hemodynamic stability and the absence of bleeding. However, many patients are currently removed from mechanical ventilation within 3 to 6 hours of arriving in the postoperative care unit (fast tracking), if appropriate criteria have been met (see **Box 54.11**).²¹¹

In planning for fast tracking, it is important to limit the use of narcotics and muscle relaxants during the surgery to a minimum and that administration be timed appropriately.

A majority of patients undergoing cardiac surgery indeed are extubated within a few hours of reaching the ICU. Multiple risk factors are responsible for prolonged intubation in patients that do require prolonged ventilator support. These factors include emergency procedures, low preoperative LVEF, advanced age, preoperative renal compromise, prolonged aortic cross-clamp time, hyperglycemia, recent MI, current smoking, and FEV₁ of less than 70% predicted.^{211,212}

Pulmonary-related reasons for the inability to wean from mechanical ventilation include noncardiogenic pulmonary edema, pneumonia, severe COPD, ARDS, and pulmonary embolism. Nonpulmonary complications such as persistent postoperative bleeding, neurologic complications (including stroke and delirium), renal insufficiency or failure, gastrointestinal complications, and sepsis also may result in a need for prolonged mechanical ventilation. In a large study of ventilator dependency (i.e., ventilation for >72 hours) after cardiac surgery, survival was 76% at 30 days, 49% at 1 year, and 33% at 5 years.²¹³

Furthermore, strategies to avoid ventilator-associated pneumonia should be employed. These include formal infection control programs, handwashing, maintaining adequate endotracheal tube cuff pressure, avoiding gastric overdistention, semirecumbent positioning of the patient, scheduled drainage of condensate from ventilator circuits,

daily sedation "vacation," adequate nutritional support, early removal of endotracheal and nasogastric tubes, and avoiding unnecessary reintubation.^{210,211}

Pain management should be included in postoperative efforts to minimize pulmonary complications. Sternotomy pain may limit the patient's ability to cough and perform deep breathing exercises, and incisional leg pain resulting from saphenous vein harvesting may prevent early ambulation, thus increasing the risk of pulmonary complications. The reader is referred to the later section on pain after cardiac surgery for other options for improving postoperative pain control and thereby minimizing splinting and complications such as lobar collapse, pneumonia, and increased duration of hospitalization.

Metabolic Disturbances

Metabolic disturbances after CPB can be highly varied and include derangements in the levels of calcium, potassium, magnesium, abnormal glucose metabolism, and alterations in urine output and temperature control.

Electrolyte Imbalance. After CPB, levels of calcium, potassium, and magnesium are usually lower due to hemodilution. Hypocalcemia can occur after CPB, particularly in bleeding patients who are receiving multiple blood transfusions with large amounts of citrate. This phenomenon is exacerbated by hypothermia and low-output states. Hypocalcemia should be corrected because it may reduce cardiac contractility. Routine administration of calcium is not encouraged however,²¹⁴ due to the possibility of reperfusion injury and possible spasm of the IMA graft.^{214,215} There is also a possibility of decreased ventricular wall compliance and an acute rise in SVR as a result of a bolus dose of calcium.²¹⁶ The most commonly used agent for replenishment of calcium is 10% calcium chloride, given in small doses while monitoring the patient's blood pressure.

Hypokalemia in the immediate postbypass period is seen secondary to either diuretic therapy, mannitol therapy, or to insulin therapy for control of glucose during surgery. If an insulin infusion is used during CPB to control glucose, it is recommended that careful and frequent monitoring of glucose and potassium take place. Generally, insulin needs are less toward the end of CPB and the infusion rate can be decreased during this time to avoid hypoglycemia and hypokalemia. Depending on the level of potassium, replenishment may be needed and should be performed, as the post-CPB myocardium is exquisitely sensitive to hypokalemia. Hypokalemia contributes to increased automaticity and may lead to atrial or ventricular arrhythmias. Therefore, hypokalemia should be corrected by the carefully monitored administration of potassium through an infusion pump at a rate of 10 to 20 mEq/h, with frequent measurement of potassium, as well as glucose and arterial blood gases.

Hyperkalemia is another possibility in the postbypass period. Common etiologies can be secondary to impaired renal function or cardioplegia administration during CPB. Occasionally, hyperkalemia is severe enough to interfere with conduction. Usual strategies to counter hyperkalemia (hyperventilation, insulin, bicarbonate, diuresis, calcium) are effective in restoring potassium to normal levels.

Magnesium levels may also be low in the post-CPB period. Usual etiologies include hemodilution with magnesium-free fluids or diuresis; the presentation may be new dysrhythmias, ventricular dysfunction, or ischemia. If hypomagnesemia is suspected, and a magnesium level cannot be obtained in a short period of time, it is recommended that magnesium be replaced in the dose of 1 to 2 grams over 15 minutes.²¹⁷ Many centers routinely administer 2 to 4 g of magnesium during weaning or after CPB in an attempt to minimize the incidence of ventricular and atrial arrhythmias.

Hyperglycemia. Hyperglycemia is extremely common after CPB (see the earlier section on the endocrine system). Poor perioperative glycemic control in patients undergoing CABG is associated with increased morbidity and mortality.²¹⁸ In patients with diabetes, maintaining serum glucose less than or equal to 180 mg/dL during CABG reduces morbidity and mortality, lowers the incidence of wound infections, reduces hospital length of stay, and enhances long-term survival. In nondiabetic patients undergoing CABG surgery, maintaining serum glucose at less than 180 mg/dL has also improved perioperative outcomes. Current recommendations from the STS are to maintain a blood glucose of less than 180 mg/dL^{219,220} in the early postoperative period and at less than 150 mg/dL in patients who require more than 3 days of ICU care as a result of ventilator dependency, the need for inotropes, mechanical device support, antiarrhythmic drugs, or renal replacement therapy.²¹⁸ There has been considerable debate over how tight to control blood glucose in these patients. Poor control has been linked with adverse outcomes, yet tight control of glucose was shown to cause a significant rise in the incidence of stroke in cardiac surgical patients²¹⁹ and was more prone to cause hypoglycemia consequences.

Treatment strategies for the control of glucose vary from institution to institution. Often an insulin infusion is started during the surgery with close monitoring of the blood glucose. If an insulin infusion is used, it is important that it be reduced as CPB is terminated so as to avoid hypoglycemia that may occur after CPB is weaned. Intravenous insulin boluses can also be used in addition to or instead of an infusion. In addition, since insulin causes potassium to migrate from the extracellular to the intracellular space, potassium should be carefully monitored and hypokalemia avoided.

Urine Output. Urine output can vary in the intraoperative period. This could be secondary to multiple factors. Normal or high urine output can occur in patients because they have adequate renal blood flow or in patients with compromised renal blood flow but in whom diuretic therapy has been administered. In oliguric patients, the differential diagnosis includes hypovolemia, hypoperfusion, or ischemic renal injury. In order to monitor renal function, we monitor the urine output frequently and communicate any prolonged decrease in urine output to the perfusionist and the surgical team so that timely steps can be taken to improve. Preservation of renal function is critically important in the cardiac surgery patient since adverse renal outcomes are associated with increased morbidity in the postoperative period.

Hypothermia. Although cardiac surgical patients are weaned from CPB after an appropriate period of rewarming and when the patient's temperature is close to 37°C, a drop in temperature is observed in the post-CPB period, called "afterdrop."²²¹ Hypothermia can lead to myocardial dysfunction, coagulopathy, and delayed metabolism of medications.

In order to prevent hypothermia, measures can be taken to prevent the afterdrop commonly seen after the patient is successfully separated from CPB. Careful monitoring of temperature is employed and measures that can be employed include the use of warm fluids, a forced air warming blanket, and raising the room temperature.

Pain

Pain after cardiac surgery can have many sources, including the sternotomy incision, chest tubes, vascular cannulation sites, and leg incisions (see also Chapter 81).²²² Chest surgical procedures through thoracotomy are especially debilitating because of pain and consequent respiratory dysfunction.²²³ Some of the deleterious effects of postoperative pain after cardiac surgery are caused by the stress response and resultant inflammation and enhanced sympathetic tone, which can increase the heart rate, PVR, myocardial work, and myocardial oxygen consumption, all leading to myocardial ischemia.

Pain after cardiac surgical procedures can also cause respiratory complications related to diaphragmatic dysfunction. Moreover, the patient's pain may cause voluntary reduction of muscular movement in the thorax and abdomen, a phenomenon often described as "splinting," which may interfere with the patient's ability to cough and clear secretions. However, at present, evidence to state definitively that any postoperative analgesic technique significantly affects morbidity or mortality after cardiac surgery is insufficient.²²⁴

Unrelieved pain does have psychological effects. Pain-related anxiety, depression, and sleep deprivation may contribute to delirium in patients in the intensive care setting. A primary benefit of effective pain control is patient satisfaction. So-called fast-track anesthesia, entailing earlier extubation, a relatively brief stay in the ICU, faster discharge from the hospital, and lower overall cost, has become a standard of care for the cardiac anesthesiologist. Effective pain control probably helps achieve these goals.

Opioids remain the gold standard for pain control after cardiac surgery, but these drugs have side effects that include nausea, vomiting, urinary retention, decreased gastric motility, pruritus, sedation, and respiratory depression. A meta-analysis showed small incremental benefits for morphine analgesia that was patient controlled compared with nurse controlled in the treatment of postoperative pain after cardiac surgery.²²⁵

Intrathecal and epidural local anesthetics and narcotics have increasingly been used to improve analgesia in patients undergoing cardiac surgical procedures. However, neither meta-analyses nor randomized trials of central neuraxial analgesia in cardiac surgical patients have shown that these techniques improve outcome.^{226,227} Nevertheless, in some studies, thoracic epidural analgesia did significantly reduce pain and the risk for dysrhythmias, pulmonary complications, and time to tracheal extubation, and it reduced

analog pain scores at rest and with activity. A major concern with the use of intrathecal, and particularly epidural, analgesia in cardiac surgery is the administration of anti-coagulation during the operation and consequent fear of spinal cord damage from a possible epidural hematoma,²²⁷ although the incidence is reported to be rare. Other techniques include the use of bilateral single-shot paravertebral blocks²²⁸ or intercostal nerve blocks followed by a subcutaneous continuous infusion of local anesthetic agents.²²⁹

Because all analgesics have side effects, some authors have suggested that it is better to use combinations of drugs or techniques (i.e., multimodal analgesia; see also Chapter 72). Although a multimodal approach to pain control after cardiac surgery is advocated, use of cyclooxygenase-2-selective inhibitors and nonselective NSAIDs remains contraindicated after cardiac surgery because of risk of thromboembolic events.²³⁰

Bleeding and Coagulopathy

Although inadequate surgical hemostasis is a common reason for blood loss after CPB, coagulopathy resulting from excessive contact activation, platelet dysfunction, and fibrinolysis can occur and must be excluded. Historically, the most common causes of excessive bleeding in cardiac surgical patients have been related to platelet activation, platelet consumption, and hyperfibrinolysis induced by the extracorporeal circuit. Despite the use of high-dose heparin, thrombin generation remains ongoing during CPB. This results in microvascular coagulation and fibrinolysis and has deleterious effects on platelet function.²³¹ In the current era, viscoelastic testing can be employed to help differentiate the causes of post-CPB bleeding among themselves and to distinguish coagulopathy from surgical sources of bleeding.

Patients who are taking antithrombotic or anticoagulant medication before cardiac operations constitute yet another subset of patients at risk for post-CPB bleeding. When possible, information should be obtained preoperatively about the degree of platelet inhibition so that if a patient is bleeding after CPB, the degree to which anti-platelet drug therapy may be a factor can be ascertained.²³² Chen and Teruya found that preoperative testing of platelet function using one POC platelet function monitor can identify patients at highest risk for perioperative bleeding; other monitors of platelet function can be used similarly.²³³

An evidence-based approach to the diagnosis and treatment of residual post-CPB microvascular bleeding entails the timely detection and treatment of specific causes of coagulopathy.²³⁴ Patients with postoperative bleeding benefit from POC testing incorporated into a transfusion algorithm that uses pharmacologic and transfusion therapies. Algorithms are designed to minimize unnecessary and indiscriminate blood product transfusion.²³⁵⁻²³⁷

Transfusion to treat coagulopathy or anemia is sometimes indicated, but it carries a cost in terms of healthcare resources and patients' outcomes. A study of more than 1900 cardiac surgical patients found that patients who received transfusions had a 70% increased risk of death and a doubling of their 5-year mortality rate, after adjustment for comorbidities, compared with patients who received no transfusions.⁷⁷ A multinational study showed that differences in transfusion practices among countries may

account for differences in outcomes.²³⁸ A study of 10,000 patients who underwent CABG from the Cleveland Clinic database confirmed the association of transfusion with early and late (i.e., 10-year) mortality; this study used a balancing score to account for confounding.²³⁹ In addition, Marik and Corwin performed a meta-analysis of 45 trials that examined complications of transfusion therapy and found that mortality was increased in transfused patients (odds ratio, 1.7, 95% confidence interval, 1.4-1.9).²⁴⁰

Guidelines and Recommendations. The STS and the SCA published a joint statement in 2007 and an update in 2011 regarding practice guidelines for transfusion and blood conservation in cardiac surgery.^{77,241} They noted six factors that appear to be important predictors of blood product transfusion in cardiac surgery:

1. Advanced age
2. Low preoperative RBC volume (i.e., preoperative anemia or low body surface area)
3. Preoperative antiplatelet or antithrombotic medications
4. Complex or redo operation
5. Emergency operation
6. Noncardiac comorbidities

The Task Force gave specific recommendations on blood conservation that included the following five points²⁴¹:

1. Consideration should be given to the use of drugs that either increase preoperative blood volume (e.g., erythropoietin) or decrease postoperative bleeding (e.g., anti-fibrinolytic drugs).
2. Techniques of conserving blood, including cell saver sequestration and retrograde priming of the pump, should be included in the operative plan.
3. To spare the patient's blood from the insult of CPB, normovolemic hemodilution or platelet-rich plasmapheresis can be considered.
4. Institutions should implement transfusion algorithms supported with POC testing.
5. A multimodal application of all of the previously mentioned guidelines is the best way to conserve blood.

These recommendations are parallel to and completely congruous with the tenets of patient blood management, which is a novel approach to blood transfusion that focuses on patient-centered therapies. The three pillars of patient blood management are as follows:

1. Preoperative optimization of RBC mass
2. Perioperative minimization of RBC loss
3. Perioperative optimal treatment of anemia

DEFINITION OF BLEEDING AND TRANSFUSION TRIGGERS. The decision to transfuse the cardiac surgical patient is one that should be made with great caution and careful consideration because allogeneic transfusion has several associated risks. The excessively bleeding patient who has a surgical source of bleeding should be carefully assessed, and often, allogeneic blood products are required to maintain hemoglobin and the integrity of hemostasis until the source of bleeding is found. Patients who have excessive microvascular bleeding from a coagulopathic cause should have careful testing of the hemostatic system, usually with POC monitoring, to assess which blood products or pharmacologic products are

needed. The problem in defining a trigger for transfusion is the ambiguity of the definition of bleeding. Many sources state that excessive chest tube drainage can be defined as more than 250 mL of bleeding per hour for at least 2 consecutive hours, or 300 mL of bleeding in a single hour. In addition to defining the severity of bleeding, these criteria also often help clinicians determine whether to return the patient to the operating room for surgical exploration.

Knowing when to transfuse RBCs is equally challenging because the triggers for transfusion often rely on hemoglobin level, which is a poor surrogate for tissue oxygen delivery. It is well known that cardiac surgery and CPB are associated with anemia, which poses certain risks.²⁴² These risks include renal failure,²⁴³ other end-organ morbidity, and even mortality,²⁴⁴ all of which have been demonstrated observationally in well-designed multivariate analyses. However, the lowest tolerable hemoglobin level clearly differs among patient populations and remains ill-defined in the literature. Nevertheless, the STS/SCA guidelines for blood conservation provide a framework for transfusion triggers within which most patients are treated appropriately. These triggers include a hemoglobin level of at least 6 g/dL during CPB and 6 to 7 g/dL before and after CPB.²⁴¹ However, underlying comorbidities can and do raise the minimum safe hemoglobin or hematocrit level.

If only standard laboratory testing is available, monitoring the coagulopathic patient in the operating room is limited to monitoring hemoglobin concentration, prothrombin time or international normalized ratio, activated PTT, platelet count, and levels of fibrinogen and fibrin degradation products. These parameters are of limited utility in the post-CPB patient because they do not interrogate platelet function and because their turnaround time is too slow to allow timely initiation of therapy. For these reasons, without POC testing of hemostasis, transfusion therapy is often initiated empirically and indiscriminately.

The platelet count provides quantitative information about platelet concentrations but little, if any, qualitative information about platelet function. Even platelet counts lower than 50,000/ μ L do not correlate with postoperative bleeding. Laboratory measures of platelet function, including bleeding time, aggregometry, and cytometry, are not rapid (requiring > 1 hour to produce results) and therefore are impractical for obtaining timely information

intraoperatively. When unacceptable microvascular bleeding occurs, no matter what the platelet count, CPB-induced platelet dysfunction is often assumed to be the culprit; however, platelet function can now be measured at the point of care.

POC monitors may be able to provide more timely information about the coagulation cascade than can laboratory measures and to assess the dynamic nature of platelet function sequentially. Such monitors are designed to test segments of the hemostatic system. The viscoelastic tests are dynamic measures of whole blood clot formation and can measure platelet integrity and the strength of the platelet-fibrinogen bond. These tests include thromboelastography (TEG; Haemonetics, Braintree, MA), Sonoclot (Sienco, Arvada, CO), and rotational thromboelastometry (ROTEM; Tem Innovations GmbH, Munich, Germany). The response of platelets to an agonist stimulus is another means of measuring platelet function. Platelet function can be measured at the point of care in this manner by the Platelet Function Analyzer-100 (PFA-100; Siemens Healthcare, Malvern, PA), Plateletworks (Helena Laboratories, Beaumont, TX), VerifyNow (Accriva Diagnostics, San Diego, CA), and the Multiplate analyzer (Roche Diagnostics, Rotkreuz, Switzerland).²⁴⁴ POC monitors have also shown promise in stratifying bleeding risk for patients who come to the operating room after receiving antithrombotic drugs, such as clopidogrel, prasugrel, or Gp IIb/IIIa receptor inhibitors.²⁴⁵⁻²⁴⁹ Finally, POC monitors provide data to support the implementation of institutional policies and practices directed at blood conservation and transfusion in cardiac surgical patients.²⁴¹

POINT-OF-CARE ALGORITHMS. The STS/SCA blood conservation guidelines strongly encourage multimodal efforts to reduce transfusion rates and conserve blood products (see also Chapters 49 to 50). Studies that used transfusion algorithms paired with POC data to guide therapy have found these measures to be both efficacious and cost effective.^{76,241} Examples of standard POC algorithms, one using the TEG and one using the ROTEM, are shown in Figs. 54.12 and 54.13, respectively. Algorithms can be constructed to incorporate any particular dynamic POC monitor or monitors.²⁵⁰⁻²⁵⁶ Studies that have incorporated many different varieties of POC tests have generally shown a reduction in or even the

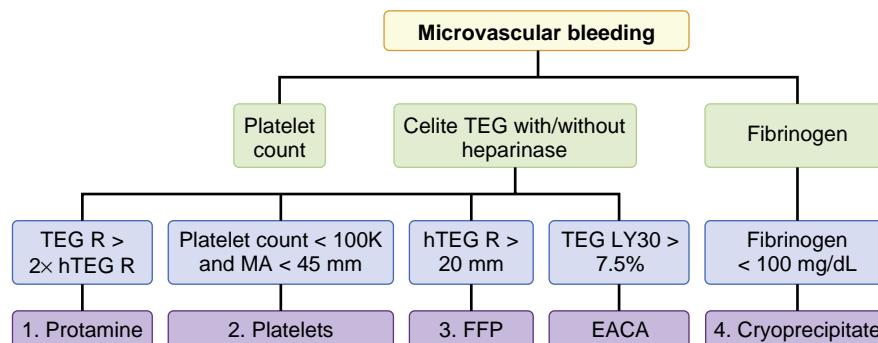


Fig. 54.12 Algorithm for transfusion requirements in the thromboelastography (TEG) group in a study. Once bleeding was diagnosed, patients received transfusions based on the results of tests in the algorithm. Based on the assumption that bleeding is often platelet related and on the finding that the platelet count and TEG results return promptly, therapy was given in the numbered order of priority. EACA, ϵ -Aminocaproic acid; FFP, fresh-frozen plasma; hTEG, heparinase-activated TEG; LY30, lysis index at 30 minutes; MA, maximum amplitude; R, reaction time. (From Shore-Lesserson L, Manspeizer H, DePerio M, et al. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg*. 1999;88:312-319.)

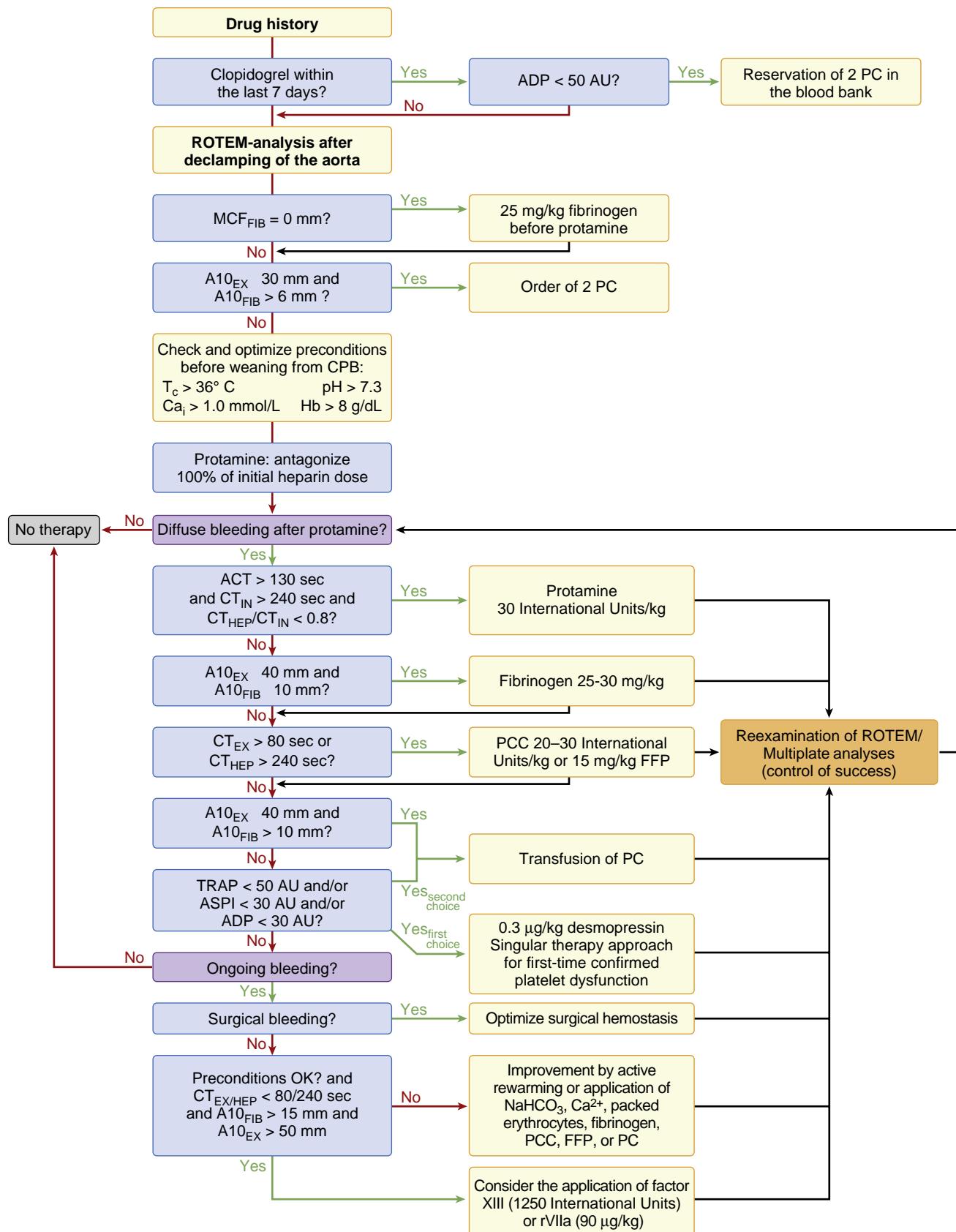


Fig. 54.13 Hemostatic therapy algorithm using point-of-care testing. ACT, Activated clotting time; ADP, ADPtest; ASPI, ASPItest; AU, aggregation unit; A10, amplitude of clot firmness 10 minutes after clotting time; Ca²⁺, calcium; Ca_i, ionized calcium; CPB, cardiopulmonary bypass; CT, clotting time; EX, EXTEM; FFP, fresh frozen plasma; FIB, FIBTEM; Hb, hemoglobin concentration; HEP, HEPTEM; IN, INTEM; MCF, maximum clot firmness; NaHCO₃, sodium bicarbonate; PC, pooled platelet concentrate; PCC, prothrombin complex concentrate; TRAP, TRAPtest. The manufacturers of ROTEM (rotational thromboelastometry) and Multiplate were Tem International GmbH and Verum Diagnostica GmbH, respectively, both of Munich, Germany. (From Weber CF, Gorlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. *Anesthesiology*. 2012;117:531-547.)

elimination of transfusions when POC is used.²⁵⁴ As a general recommendation, the POC instrument or instruments used should be able to measure some aspect of platelet function. The viscoelastic test in the TEG measures both platelet function and the platelet response to ADP and arachidonic acid. Many TEG-guided and ROTEM-guided algorithms have been studied and shown to reduce blood product use effectively in cardiac surgery-related hemorrhage. A more recent approach to POC algorithm includes using ROTEM and an algorithm that includes early treatment with fibrinogen and PCCs (see Fig. 54.13).²⁵⁷ This sort of approach to bleeding postpones the moment when allogeneic blood products are needed and thus has been successful in reducing allogeneic blood product usage. Preliminary work suggests that no increase in thrombotic events occurs with this “pharmacologic” approach to bleeding, but more large-scale studies need to be conducted before safety can be confirmed.

Pharmacologic Treatment. Pharmacologic drugs used for hemostasis in CPB are used both prophylactically to prevent hyperfibrinolysis and therapeutically to treat bleeding. Antifibrinolytic drugs are used before CPB to prevent the inevitable activation of fibrinolysis and coagulation that result from contact between blood and the extracorporeal circuit. The STS/SCA guidelines provide the strongest evidence-based support (class I) for the use of synthetic antifibrinolytic agents in blood conservation.

In structural terms, the synthetic antifibrinolytic agents are lysine analogues. They bind to plasminogen and plasmin, thus inhibiting their ability to bind to lysine residues on fibrin and thereby impeding fibrinolysis. The two synthetic antifibrinolytic agents that are used clinically are EACA (Amicar) and TA. They differ primarily in potency and elimination half-life: TA is 6 to 10 times more potent and has a longer half-life than EACA.²⁵⁸

Dose regimens for the synthetic antifibrinolytic agents are anything but standardized. Generally, the dose of EACA is a 50- to 150-mg/kg load followed by an infusion of 15 to 25 mg/kg/h; the dose of TA may be a 10- to 30-mg/kg load followed by an infusion of 1 to 15 mg/kg/h. However, many other dosing strategies are described in the literature.²⁵⁹⁻²⁶⁴

Because both EACA and TA are renally excreted, they should not be given to patients with upper urinary tract bleeding; the concentration of the drug in the renal collection system could cause thrombosis and obstructive nephropathy.²⁶⁵

Aprotinin as an antifibrinolytic agent was used as a routine part of perioperative care in cardiac surgical patients until 2006, when published reports suggested adverse outcomes that had not been found in previous randomized controlled studies.^{119,266} After several observational studies confirmed these adverse outcomes and a single randomized controlled trial suggested an increase in mortality associated with aprotinin, the FDA and other global agencies suspended the marketing of aprotinin.¹²⁰

Other pharmacologic drugs that may be used in cardiac surgical bleeding are mentioned in the STS/SCA Task Force guideline update.⁷⁶ Using desmopressin was classified as “not unreasonable” in patients with characteristics known to be responsive to desmopressin (von Willebrand factor or factor VIII deficiencies, cirrhosis, aspirin use, and

uremic platelet dysfunction).²⁴¹ Desmopressin is administered in doses of 0.3 to 0.4 µg/kg, which are usually given slowly over 20 to 30 minutes to reduce the drug’s propensity to cause hypotension. The use of recombinant factor VIIa (factor rVIIa) was reevaluated, but the published class IIb recommendation was unchanged in the update.⁷⁶ Factor VIIa use was classified as “not unreasonable” for treating intractable life-threatening hemorrhage that is unresponsive to traditional therapies.²⁴¹ A multicenter randomized trial in cardiac surgery found that patients treated with factor rVIIa had less bleeding than did control patients; however, a nonsignificant trend toward increased adverse events in the treated patients caused the study to be halted and the recommendations to proceed with caution when considering administration of this drug.²⁶⁷ Prophylactic use of factor rVIIa is not recommended in cardiac surgery.

The PCCs have evolved into a more common treatment for coagulation factor deficiencies after CPB. 4-factor PCCs that were originally marketed either for hemophilia or for warfarin reversal have been used “off-label” in transfusion algorithms in bleeding cardiac surgical patients.²⁵⁷

In summary, interdisciplinary approaches to blood conservation are vital to the care of cardiac surgical patients. Perioperative and critical care personnel must use a series of combined approaches to reduce transfusions and the adverse effects of transfusion and anemia. Important to this approach is a sound algorithmic procedure that incorporates POC testing, pharmacology, and rational blood product use to improve outcomes.

Cardiopulmonary Bypass

CPB is a form of extracorporeal (*extra* = “outside of,” *corporeal* = “the body”) circulation (ECC) in which the patient’s blood is rerouted outside the vascular system, and the function of the heart, the lungs, and, to a lesser extent, the kidneys is temporarily assumed by surrogate technology. The circuitry and equipment used to facilitate this substitution are topics of the next section of this chapter.

CIRCUITRY AND EQUIPMENT

The most common and most complicated ECC procedure is CPB. The goal of CPB is to provide a motionless and bloodless field for the surgeon by rerouting the patient’s entire CO around both the heart and the lungs. Other ECC techniques include left heart bypass (LHB), cardiopulmonary support (CPS), and extracorporeal membrane oxygenation (ECMO).

The pumps, tubing, artificial organs, and monitoring systems used in CPB are diagrammed in Fig. 54.14. Simply stated, venous blood is intercepted as it returns to the right atrium and is diverted through the *venous line* of the CPB circuit to a *venous reservoir*. The *arterial pump* functions as an artificial heart by withdrawing blood from the reservoir and propelling it through a *heat exchanger*, an artificial lung (the *oxygenator*), and an *arterial line filter* before returning it through the *arterial line* to the patient’s arterial system. Additional pumps and components are used to assist in the operation to manage shed blood (the *pump sucker*), decompress the heart (*vent*), and deliver the *cardioplegia solution*.

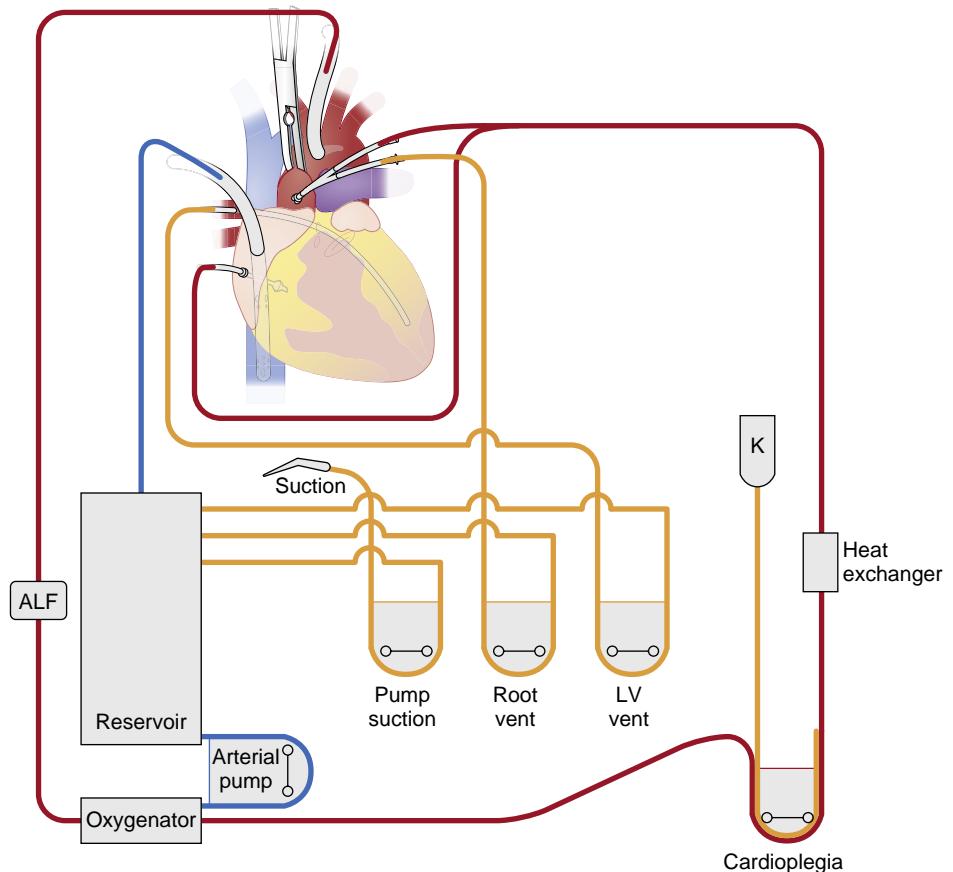


Fig. 54.14 A typical cardiopulmonary bypass circuit interfaced with a patient. ALF, Arterial line filter; K, potassium; LV, left ventricular.

Blood Tubing

The tubing used to connect the various components and conduct blood into and out of the patient's vascular system is medical-grade polyvinyl chloride. For decades, the blood-tubing interface was untreated polyvinyl chloride. However, the newer generation of polyvinyl chloride tubing has surface coatings and other modifications that significantly alter the bioreactivity of the surface. Collectively, these coatings have been shown to reduce plasma levels of markers of subclinical coagulation, attenuate the increase of cytokines and other inflammatory markers, and shorten intubation times.²⁶⁸⁻²⁷⁰

Venous Reservoirs

Blood reservoirs perform an important function in the conduct of CPB by facilitating the displacement of a large volume of blood out of the circulation at strategic times during the operation. Positioned between the venous line and the arterial pump, blood reservoirs may be collapsible plastic bags or clear plastic hard-shelled containers. Hard-shelled reservoirs include an integral filtration mechanism with a screen and depth filters through which blood must pass before leaving the outlet of the vessel. Almost universally, hard-shelled reservoirs have integrated positive- and negative-pressure release valves, which are necessary for the application of vacuum to the reservoir to augment venous drainage. If vacuum-assisted venous drainage is employed, the vacuum pressure in the reservoir should be maintained

at the minimum necessary, and entrainment of air from the surgical field into the venous line should not be permitted. Reservoir pressures in excess of 60 mm Hg have been shown to increase microbubble counts measured in the circuit's arterial infusion line dramatically.²⁷¹

Arterial Pumps

The pumping device used to replace the function of the heart generally uses one of two primary technologies: a roller pump or a centrifugal pump. Roller pumps are positive-displacement pumps that function by occluding a point in a piece of tubing and then rolling the occlusive point of contact along a length of the tubing. This process forces the fluid in the tubing to move forward in front of the occlusive point while simultaneously drawing in fluid behind the occlusive point. Centrifugal pumps, in contrast, are nonocclusive kinetic pumps that generate flow by magnetically coupling the high-speed revolution of a reusable motor to the plastic plates, fins, or channels inside a disposable cone. This process produces a constrained vortex that propels fluid through the opening on the side of the cone while drawing fluid into the point of the cone. Both pump technologies are traumatic to the formed elements in blood; however, centrifugal pumps are thought to be less traumatic than roller pumps.²⁷²

Each type of pump poses unique risks that must be appreciated. Roller pumps, by virtue of their occlusive nature, are capable of generating extremely high positive and negative

pressure and are also able to pump massive quantities of air. Consequently, the national standard of care requires that these pumps be servoregulated to reduce their speed automatically when either high pressure or air is detected in the path of the blood. In contrast, centrifugal pumps, being nonocclusive, are unable to generate extremely high or low pressure. Additionally, if a large bolus of air is introduced into the disposable cone, the air will remain in the cone, thus displacing the blood, and the pump will be unable to generate forward flow. This feature prevents centrifugal pumps from pumping large volumes of air. However, the lack of a point of tubing occlusion inside the pump allows retrograde flow from the patient's high-pressure arterial system backward through the arterial line, filter, and oxygenator and ultimately into the low-pressure venous reservoir. This situation may occur whenever the pump's revolutions per minute are reduced below a critical threshold. A large-bore one-way valve or a computer-activated electronic clamp can be positioned in the arterial line to eliminate the possibility of retrograde arterial flow and inadvertent exsanguination of the patient.

Heat Exchanger

Heat exchangers are essential to CPB because they facilitate the management of the patient's blood temperature. Throughout the period of CPB, 20% to 35% of the patient's circulating blood volume is outside the body and is exposed to the ambient temperature of the operating suite, which can cause hypothermia. Therefore, in all CPB procedures, an inherent need exists to warm the blood before CPB is terminated. Additionally, for many surgical procedures, some amount of hypothermia, from mild (35°C) to profound (18°C), is desirable to reduce the patient's metabolic rate. In these cases, the heat exchangers may be used to reduce the temperature of the blood when CPB is initiated and then to warm the blood before CPB is terminated.

Oxygenator

The oxygenator substitutes for the patient's native lungs and performs the essential function of gas exchange. Several similarities exist between the native lung and the oxygenator: both have a gas space and a blood space, both are driven by passive diffusion gradients, and both use a membrane to separate the blood from the gas. In the oxygenator, the membrane is usually made from microporous polypropylene. This material is extruded into thin straws with an outer diameter of 200 to 400 μm , a wall thickness of 20 to 50 μm , and a total surface area of 2 to 4 m^2 . Typically, oxygenators have a static priming volume of 135 to 340 mL and are capable of arterializing up to 7 L/min of typical venous blood.²⁷³

The native lung uses the conductive airways for both inspiration and expiration and depends on a certain tidal volume and respiratory rate to refresh the gas in the alveolar space regularly. The oxygenator, however, has separate gas inlet and outlet ports and can refresh the gas inside its gas space (the internal lumen of the straws) with a continuous flow or "sweep" of gas through the oxygenator. The blood space of an oxygenator is the space around the outside of the straws. Venous blood entering the oxygenator is directed across the outside of the fibers while gas is concurrently circulated through the inside of the fibers. Pressure

gradients between the blood space and the gas space drive oxygen across the membrane and into the blood, whereas carbon dioxide is driven out of the blood and into the gas phase. Similarly, volatile anesthetic agents can be delivered to the patient through the oxygenator's sweep gas. Unlike the membrane in the native lung, however, the oxygenator's membrane is not a true membrane. The microscopic (0.5- to 1.0- μm) pores on the sides of the fibers are small enough to prevent plasma and the formed elements of blood from leaking through but are still large enough to allow gas to pass through. Therefore, care must be taken to ensure that the pressure in the gas space never exceeds the pressure in the blood space, or gaseous emboli will form in the blood. In appreciation of the risks inherent in using a pressurized gas space, most oxygenators are designed with multiple gas outlet ports. In any case, caution should be exercised to ensure that the outlet of the gas phase cannot become occluded.

Arterial Line Filter

In the United States, arterial line filters are used in more than 95% of CPB procedures in adults. These filters are placed in the arterial line as the last component through which blood passes before it returns to the patient. With pore sizes of 20 to 40 μm , arterial line filters increase the patient's safety by removing particulate and gaseous microemboli. To remove bubbles from the blood path effectively, arterial line filters must be continuously "purged" by allowing a small amount of blood to recirculate from the top of the filter back into the venous reservoir. Many ECCs are designed to capitalize on this continuous arterial shunt with the incorporation of a flow-through blood gas sensor that continually monitors the blood gas concentrations in the postoxygenator blood. These in-line blood gas measurements are generally reliable and can be used for the early identification of trends and precise management of oxygenator performance.

SEQUENCE OF EVENTS

Although the approach to surgical procedures that require CPB varies among institutions, all procedures loosely follow a predictable sequence of events. At any institution, CPB requires circuit selection and priming, anticoagulation, cannulation, initiation and maintenance of CPB, myocardial protection, and finally, weaning and termination from CPB.

Circuit Selection and Priming

When selecting the components for an extracorporeal circuit, the perfusionist first calculates the highest blood flow that may be necessary during the procedure. Typically, the highest blood flow is approximately 2.4 to 3.0 L/min/ m^2 or 60 to 70 mL/kg/min. The calculated flow is then compared with the rated flow for the components of the ECC circuit. This flow rating represents the highest blood flow rate at which the component can perform its function within the acceptable range of hydraulic forces (pressure and shear stress) without causing an unacceptable amount of blood trauma.

The combination of components included in the ECC determines the prime volume of the circuit, or the volume of balanced electrolyte solution necessary to de-air the circuit

BOX 54.12 Resultant Hematocrit Formula

$HCTr = \text{Patient's preoperative red blood cell volume} / \text{Total volume of distribution at the start of CPB}$

$$HCTr = (BVp \times HCT) / (BVp + PVc)$$

$$HCTr = (kg \times 75 \times HCT) / (kg \times 75) + PVc$$

where

$HCTr$ = resultant hematocrit

BVp = patient's blood volume

kg = patient's weight in kg

PVc = prime volume of the extracorporeal circuit

CPB, Cardiopulmonary bypass.

completely. This prime volume is the main cause of the hemodilution associated with CPB. Therefore, the perfusionist must calculate the patient's resultant hematocrit ($HCTr$), which is the patient's predicted hematocrit after the patient's preoperative blood volume is mixed with the asanguineous prime volume of the ECC. The $HCTr$ is computed by dividing the patient's calculated volume of RBCs into the calculated total volume of distribution represented by the addition of the ECC prime volume to the patient's blood volume (Box 54.12). An adult patient's intravascular volume of distribution will increase by 20% to 35% when CPB is initiated. This increased volume of distribution dilutes not only all the proteins and formed elements of the blood but also plasma levels of drugs. If this dilution is not anticipated, the patient's depth of anesthesia and circulating concentrations of many pharmacologic drugs may be reduced when CPB is initiated.

The solution used to prime the CPB circuit is generally a balanced electrolyte solution containing normal plasma concentrations of many of the standard blood ions. Various drugs may be added to the solution to attenuate the dilutional effect of CPB on those ions (e.g., albumin, heparin, bicarbonate) or to discourage edema formation or encourage diuresis of the prime fluid by the patient (e.g., mannitol).

Anticoagulation

With the circuit primed and the vessels exposed, standard procedure requires that the patient be fully anticoagulated before cannulation. Dosing of heparin and monitoring of the ACT are discussed earlier in this chapter. Many commercial devices are designed to monitor the ACT, and although the ACT is used as if it were a standardized test, the results produced by different instruments are far from standardized. These devices, when used on the same pool of heparinized blood, can produce ACT results that vary by as much as 40% (see Fig. 54.7).

The ACT test is not used to monitor heparin levels but to monitor the anticoagulant effects of heparin and other anticoagulants. Thus, elevated ACT measurements taken before, during, or after CPB may be influenced by variables other than heparin (e.g., hypothermia, hemodilution, coagulopathy, and anticoagulants).

Some studies suggest that subclinical coagulation may progress despite acceptable ACT times during CPB and that maintaining higher circulating heparin levels may reduce this process.^{88,274} POC heparin level tests are commercially available and may be used to monitor circulating heparin levels in CPB-supported patients. Indeed, some centers

monitor both the circulating level of heparin and its anti-coagulant effects and administer heparin intermittently throughout the procedure to maintain a predetermined therapeutic heparin level, as well as a minimally acceptable ACT.

Heparin dosing may be based on the patient's weight (300–400 units/kg) or determined by a dose-response curve. Heparin dose-response curves are determined *in vitro* by measuring the ACT of the patient's blood at baseline (without heparin) and after a known concentration of heparin (2.5 units/mL) is added. By graphing the ACT in seconds against the blood concentration of heparin, one can extrapolate the blood concentration of heparin needed to achieve a target ACT acceptable for CPB. Most patients need circulating blood heparin concentrations between 1.5 and 3.0 units/mL to achieve an ACT of greater than 400 seconds. Commercial devices have been designed to automate this process and calculate the heparin dose using the *in vitro* dose-response curve, however these calculated doses do not simulate the *in vivo* response to heparin and often the calculations are flawed. Most centers have adopted a weight-based heparin dosing strategy for the initiation of CPB.²⁷⁵ From the patient's height, weight, sex, and heparin dose-response test results, the machine calculates the appropriate patient-specific heparin dose to administer during CPB.

Cannulation

Every CPB procedure requires a high-flow cannula in a large vein and a cannula in a large artery for respectively withdrawing blood from and returning blood to the patient (Table 54.10). Most procedures include additional cannulas for administering cardioplegia solutions to the heart and removing (venting) blood and air from the chambers of the heart (Fig. 54.15). Different surgical procedures require different cannulation techniques, the most common of which are described here.

The target for venous cannulation is generally the right atrium. The right atrium is the central repository for all venous blood, and the RA appendage is conveniently accessible through a sternotomy. Although RA cannulation is optimal for most cardiac surgical cases, the cannula may not perform well when the heart is being retracted. Significant retraction of the heart is necessary to access some posterior coronary arteries for bypass or to access the mitral valve through a left atriotomy. Because of a need for surgical exposure or retraction involving the right atrium, the venous cannulation site for mitral valve or tricuspid valve procedures is moved out of the atrium and to the SVC and inferior vena cava (IVC). If a cannula is placed in each vena cava, venous blood can be intercepted just before it enters the right atrium so that the surgeon can have a bloodless field for operating and yet acceptable drainage is provided throughout the procedure. The right atrium may also be approached through the femoral vein. A femoral venous cannula extends the entire length of the IVC and rests with its openings in the right atrium.

An improperly sized or positioned venous cannula obstructs the flow of blood into the ECC circuit. This may elevate CVP and encourage extravasation of blood volume from the vascular compartment into the extracellular compartment (third spacing). Therefore, it is important to

TABLE 54.10 Common Approaches to Venous and Arterial Cannulation for Cardiopulmonary Bypass

Procedure	Venous	Arterial	Cardioplegia	Vent	Comments
CABG	2-stage approach in the RA	Ascending aorta	Root and/or CS	Aortic root	Patients with low EF or failure to wean from CPB may benefit from LV venting
AVR	2-stage approach in the RA	Ascending aorta	Root and/or CS, plus handheld selective once the root is open	LV and aortic root	None
MVR	Bicaval	Ascending aorta	Root and/or CS	LV and aortic root	None
Aortic root replacement, not including the arch	2-stage approach in the RA	Ascending aorta	Root and/or CS	LV and aortic root	The closer the repair is to the head vessels, the more difficult aortic cannulation becomes
Aortic arch	2-stage approach in the RA	Axillary or femoral artery	Root and/or CS	LV and aortic root	CS cardioplegia unlikely if the coronaries are unobstructed
Redo procedures	Femoral vein	Femoral artery	Root and/or CS	Aortic root and/or LV	Only in extreme cases (i.e., when the heart is tightly adhered to the back of the sternum, or any time that the heart is lacerated during sternotomy)
Other intracardiac procedures	Bicaval	Ascending aorta	Root and/or CS	LV and aortic root	Any procedure that requires opening the RA or excessive surgical retraction

AVR, Aortic valve repair or replacement; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; CS, coronary sinus; EF, ejection fraction; LV, left ventricle; MVR, mitral valve repair or replacement; RA, right atrium.

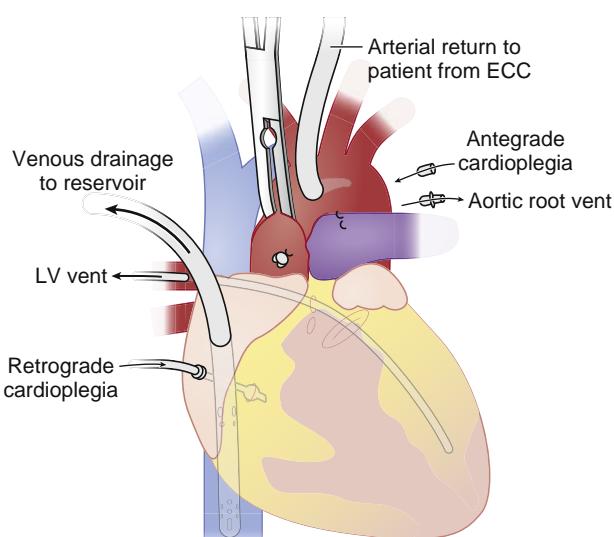


Fig. 54.15 A common cannulation approach for cardiopulmonary bypass (CPB) procedures. Two cannulas are necessary to provide CPB. A cannula in the right atrium provides venous drainage to the extracorporeal circuit (ECC), and an arterial cannula placed in the ascending aorta allows arterial return to the patient from the ECC. Additional cannulas are necessary to protect the heart after cross-clamping. Cardioplegia can be administered in antegrade fashion through a special needle placed in the ascending aorta between the aortic valve and the aortic cross-clamp. Retrograde cardioplegia can be delivered directly into the coronary sinus through a special balloon-tipped cannula. Vent cannulas are used to decompress the heart while the aorta is clamped and to remove bubbles before cross-clamp removal. The aortic root vent is integrated into the antegrade cardioplegia needle, and the left ventricular (LV) vent cannula is inserted through the right superior pulmonary vein.

evaluate the performance of the venous cannula or cannulas when CPB is initiated. Properly placed venous cannulas allow complete decompression of the right side of the heart, as indicated by a CVP and PAP of zero and a nonpulsatile arterial blood pressure.

The ECC returns oxygenated blood to the patient through the arterial cannula. For CABG and valve procedures, the standard target for the arterial cannula is the portion of the ascending aorta below the aortic arch but 3 to 4 cm above the aortic valve. The alternative approaches of axillary or femoral artery cannulation are used in procedures that require the manipulation of much of the aortic root, arch, or both. Axillary artery cannulation is generally facilitated by the anastomosis of a tube graft to the side of the axillary artery to provide access for the arterial cannula without interrupting blood flow to the right arm. An added benefit of axillary cannulation for aortic arch procedures is that clamping the innominate artery allows antegrade cerebral perfusion to be performed during a period of circulatory arrest. Femoral arterial cannulation involves inserting the cannula through the femoral artery and into the abdominal aorta. Blood flow to the thorax is directed in retrograde fashion upward into the aorta. Ischemia of the cannulated limb is a risk commonly associated with femoral arterial cannulation, and dissection of the cannulated artery is a risk associated with the cannulation of any arterial site. Iatrogenic aortic dissection at the cannulation site occurs in approximately 200 procedures annually in the United States, with a resultant mortality of 48%.²⁷⁶ Proper cannula placement and patency should be confirmed before CPB is initiated.

With venous and arterial cannulas in place, the heart and the lungs can be bypassed. However, additional

cannulas are needed to facilitate aortic cross-clamping and cardioplegic arrest. For example, cardioplegia cannulas can be placed in the ascending aorta, and then the aorta can be occluded by placing a large vascular clamp (i.e., a cross-clamp) across it. Occluding the aorta between the arterial cannula and the antegrade cardioplegia cannula interrupts blood flow from the arterial line of the ECC to the coronary arteries, thereby initiating a period of global myocardial ischemia. Intermittent or continuous administration of cardioplegia through the antegrade and retrograde cardioplegia cannulas (see Fig. 54.15) serves to attenuate the ischemic insult (by a mechanism discussed later).

Bronchial pulmonary vascular connections deliver approximately 1% of the CO to the lungs, from where it is subsequently returned to the left side of the heart. In patients with chronic pulmonary disease, this recirculation may increase to more than 10% of CO. During the period when the aorta is cross-clamped, this blood volume will distend the left side of the heart and the pulmonary vasculature if the blood is not actively removed. Additionally, intracardiac procedures inherently introduce air into the left-sided chambers, and this air must be removed before the patient is weaned from CPB.

Vent cannulas facilitate decompression and de-airing of the heart. The heart is most commonly vented at the aortic root or directly from the LV. Aortic root vents use the same cannula that is used to deliver antegrade cardioplegia (see Fig. 54.15) and draw blood and air from the LV across the aortic valve and into the reservoir of the ECC circuit. Because the antegrade cardioplegia needle has a small gauge and is positioned above the aortic valve, root vents have a couple significant limitations: they cannot be used when antegrade cardioplegia is being administered, and they are ineffective in decompressing the LV when the cross-clamp has been removed. These limitations are not generally significant during an uncomplicated CABG procedure, but for CABG in patients with severely compromised ventricular function and for all intracardiac procedures, direct LV venting becomes essential. Typically, LV vents are introduced through the right superior pulmonary vein and are advanced through the left atrium, across the mitral valve, and into the LV (see Fig. 54.15). The 10- to 14-Fr cannula used for this purpose offers significantly better venting capacity than does the root vent. Flows in the range of several liters per minute can be drawn through these cannulas when necessary, and because these cannulas are inserted directly inside the LV, they are very effective in removing air bubbles that remain after an intracardiac procedure has been completed. Additionally, because the LV vent is separate from the cardioplegia cannula, it can be used to decompress the heart during antegrade cardioplegia administration, which may be necessary for patients with aortic insufficiency. Unfortunately, numerous case reports exist of injuries to patients that resulted from air being pumped into the heart through malfunctioning vent lines. The proper function of the vent pump should be confirmed at the field before the pump is connected to the patient.

Initiation and Maintenance of Cardiopulmonary Bypass

Once anticoagulation is confirmed and cannulation is performed, CPB may be initiated. Before initiating CPB, it is good practice to verify the patency of the arterial cannula.

After the proper position of this cannula is confirmed, CPB may be initiated by removing the clamps on the venous line between the venous cannula and the reservoir. The patient's blood then passively drains into the ECC. Simultaneously, the arterial pump on the CPB machine begins to infuse the mixture of prime solution and autologous blood into the patient through the arterial cannula. Evaluating the performance of the venous and arterial cannulas is very important during the initial seconds of CPB. The pressure in the arterial line of the ECC should be maintained at less than 300 mm Hg to prevent excessive trauma to the formed elements of the blood. Venous cannula position is evaluated mainly by examining the patient's hemodynamics. Provided the venous cannula is adequately draining the venous return to the heart, right-sided heart pressure (CVP and PAP) should decrease to 0 mm Hg, and the arterial blood pressure should reach a normal mean pressure (50–90 mm Hg) while also becoming nonpulsatile.

The arterial trace usually becomes nonpulsatile as the heart is emptied and the pumping force is changed from the ventricle to the nonpulsatile heart and lung machine. However, patients with aortic insufficiency continue to have a pulsatile arterial trace despite complete venous drainage (CVP and PAP = 0 mm Hg) because of regurgitation of blood from the arterial cannula across the incompetent aortic valve and back into the LV. If right-sided heart pressure does not reduce to 0 mm Hg, the arterial trace remains pulsatile, and arterial pump flow cannot be increased to full flow; in that case, the position of the venous cannula must be reevaluated. Once full flow has been achieved, the function of the heart and lungs will have been completely transferred to the CPB machine; the anesthesiologist then can turn off the ventilator, and hypothermia of the patient can be initiated.

The initiation of CPB is often associated with a period of hypotension, which can be managed with the administration of an α -agonist (e.g., phenylephrine) into the venous reservoir of the ECC circuit (Fig. 54.16). Although it is common for cerebral oximetry values to reduce transiently at this point, acutely reduced cerebral oximetry values on CPB initiation may provide the first indication of poor SVC drainage or selective perfusion of a single aortic head vessel.^{277–279} Markedly changed cerebral oximetry values warrant additional confirmation of cannula position and function. While CPB is maintained, the adequacy of perfusion is continuously evaluated by monitoring hemodynamic variables. Blood flow from the arterial pump can be manipulated across a range of 1.6 to 3.0 L/min/m² to deliver an arterial blood pressure of 50 to 90 mm Hg and maintain SvO_2 greater than 65%. Any hypotension or hypertension that occurs despite adequate flow and SvO_2 can be treated by adjusting the patient's SVR with vasoconstrictors or vasodilators.

Blood samples should be taken at least every 30 minutes. Arterial blood gas is drawn to assess the performance of the oxygenator and to monitor the patient for the development of acidosis. Base deficit values of -5.0 mmol/L or less can be corrected with sodium bicarbonate, but the underlying cause of the acid production should ultimately be addressed. Increased perfusion flow and blood pressure may be indicated. ACTs are drawn to assess continued adequacy of anticoagulation and values shorter than the institutional parameter acceptable for CPB (usually ≥ 400

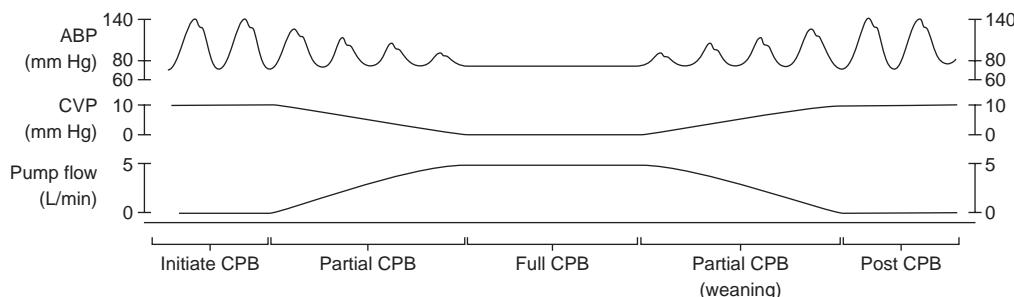


Fig. 54.16 Illustration of a patient's hemodynamics before cardiopulmonary bypass (CPB), during the initiation of CPB, during full CPB, while weaning from CPB, and after CPB. ABP, Arterial blood pressure; CVP, central venous pressure.

seconds) should be treated with a heparin bolus administered into the ECC.

Urine output is also monitored during CPB as an indicator of perfusion flow and pressure. However, poor urine production during CPB has not been shown to predict postoperative renal insufficiency. Rather, age, preoperative renal function, the duration of CPB, and EF have been correlated with postoperative renal dysfunction.²⁸⁰

Myocardial Protection

To provide a motionless field for the surgeon, the heart is arrested in diastole by the administration of a potassium-enriched cardioplegia solution. Cessation of myocardial electromechanical activity is the single most important step in reducing the heart's metabolism. Potassium-induced arrest alone reduces the heart's myocardial oxygen consumption by 90%. It is common to augment this reduction with hypothermia by administering cold cardioplegia solution. The combined influence of potassium arrest and myocardial temperatures lower than 22°C reduces myocardial oxygen consumption by 97% and enables the tissue to withstand a complete interruption of blood flow for periods of 20 to 40 minutes. Once the surgical procedure is completed, myocardial arrest can be reversed by reperfusing the coronary arteries with warm normokalemic blood.

The ingredients of cardioplegia solutions vary considerably from institution to institution, save that potassium is always used as the arrest agent. Whereas some centers may use a very simple solution of potassium-enriched whole blood, others may choose a more complex solution with a variety of chemical additives. The trend in clinical practice has been not to use purely crystalloid cardioplegia solutions; instead, most centers now use some form of blood cardioplegia. The ratio of blood to crystalloid is generally 4:1 or 8:1. The crystalloid solution is often mixed with arterialized whole blood from the ECC circuit in an exact ratio by placing two different-sized tubes (the larger drawing from the arterial line of the ECC and the smaller drawing from the bag of cardioplegia solution) through a single roller pump and splicing the two tubes together downstream from the outlet of the pump. Generically, the chemicals added to the cardioplegia solutions are designed to make the solution slightly hypertonic to reduce edema, and these chemicals include a buffer to counter the heart's production of acidic metabolites and a substrate for energy or catalysts to assist the heart in the production of adenosine triphosphate. Typically, solutions with two different potassium concentrations are used during the procedure. For inducing cardioplegic arrest, a "high-K" solution with

a potassium concentration of approximately 20 to 30 mEq is used. After isoelectric arrest is induced, the solution is changed to a "low-K" mixture with a potassium concentration of approximately 10 mEq.

These solutions can be administered in *antegrade* fashion into the coronary arteries via the aortic root, through a needle placed between the aortic cannula and the aortic valve, or in *retrograde* fashion into the coronary veins, via a balloon-tipped cannula placed in the coronary sinus. Antegrade cardioplegic delivery is the most physiologic approach. However, when the patient has pronounced CAD or aortic valve insufficiency, antegrade administration may not reach the coronary arteries uniformly and thus will not adequately deliver cardioplegia to the myocardium. In these instances, retrograde cardioplegia is used. Limitations of retrograde cardioplegia also exist however, and include the fact that the free wall of the right ventricle and the posterior onethird of the interventricular septum (the distribution territory of the right coronary artery [RCA]) are poorly perfused by retrograde delivery.²⁸¹ Additionally, the microvascular areas of the heart that are perfused by retrograde cardioplegia are less able to sustain normal myocardial energy metabolism.²⁸² Thus, the most complete technique for myocardial protection involves both antegrade and retrograde delivery. In fact, it is not uncommon for cardioplegia to be delivered simultaneously in both antegrade and retrograde fashion.

Cardioplegia is commonly administered intermittently in a volume-dosing regimen. After an initial arrest dose of approximately 1000 to 1500 mL of "high-K" solution is administered, perfusion of the heart is suspended for a period of 10 to 40 minutes while the surgeon operates on the heart. Then, periodically throughout the procedure, 200- to 500-mL doses of "low-K" solution are administered to deliver nutrients to the cells and maintain the potassium concentration. Intraoperative evaluation of the adequacy of myocardial protection is empirical and based on the quiescence of the ECG, the time since the last dose was administered, and the temperature of the heart. The filling state of the ventricular chambers should also be evaluated. If the vent lines are not keeping the heart empty, it will warm more quickly and the heart muscle will be under tension. This state increases myocardial oxygen consumption and compromises myocardial protection. To reinstitute the electromechanical activity of the heart, warm, normokalemic blood is infused into the coronary arteries. This may be done by administering a "hot shot" through the cardioplegia cannulas or by simply removing the cross-clamp.

Weaning and Termination of Cardiopulmonary Bypass

The process of weaning the patient from the heart and lung machine requires an increased level of communication and awareness among the anesthesiologist, perfusionist, and surgeon. Before weaning and termination, the patient should be rewarmed and the heart de-aired. Regular cardiac electrical activity should be confirmed and supported with a pacemaker if necessary. Ventilation of the lungs must be resumed and laboratory values confirmed and corrected if needed. By slowly reducing venous drainage to the ECC and transfusing volume from the reservoir to the patient, normal filling volume can be returned to the heart. As the CO is returned to normal, flow from the arterial pump of the heart and lung machine is decreased and eventually terminated. Immediately after the termination of CPB, the patient is often hemodynamically supported by volume replacement with the blood remaining in the ECC, frequently supplemented with vasopressors or inotropic agents (see the earlier section on weaning from CPB).

When the patient is hemodynamically stable, protamine can be administered to reverse the anticoagulatory effect of heparin. The administration of protamine to the patient is a sentinel event that must be communicated clearly by the anesthesiologist to the perfusionist and surgeon. In the event of inadvertent return of blood containing protamine to the ECC through the pump sucker, the blood remaining in the circuit may clot and render the circuit unusable for urgently reconstituting CPB. Therefore, all cannulas should be removed before the action of heparin is fully reversed, and the blood remaining in the ECC should be salvaged by centrifugation or hemofiltration for return to the patient by the anesthesiologist.

Protamine inactivates heparin by irreversibly binding with the strongly acidic heparin molecule to form a stable salt with no anticoagulant effects. POC tests are available for several ACT machines to calculate a patient-specific protamine dose.²⁸³ If an automatically generated protamine dose-response curve is not available, many institutions calculate the protamine dose needed from the total dose of heparin delivered to the patient. This calculation usually results in the administration of 1 to 1.3 mg of protamine for every 100 units of heparin given. Protamine should be administered slowly over a period of 5 to 10 minutes to reduce the risk of hypotension. After protamine administration, ACTs should return to baseline. An increased ACT may indicate residual heparin or may be the result of a coagulation deficiency that necessitates additional laboratory tests, such as coagulation panel tests, heparin assays, platelet function analysis, thromboelastography, or any combination of these investigations.

OTHER ISSUES

Temperature

Deliberate hypothermia is a reliable method of neuroprotection and is often used during routine CPB. Deep hypothermia unquestionably confers cerebral protection when the circulation must be arrested during cardiac surgery. Even mild hypothermia (as little as 1°C-2°C) minimizes the severity of cerebral ischemia in animal models. Various suggested

TABLE 54.11 Protective Effects of Hypothermia and Deleterious Effects of Hyperthermia During Cerebral Ischemia

Hypothermia	Hyperthermia
Favorable balance between oxygen supply and demand	Imbalance between oxygen supply and demand
↓ Excitotoxic neurotransmitter release	↑ Excitotoxic neurotransmitter release
↓ Blood-brain barrier permeability	↑ Blood-brain barrier permeability
↓ Inflammatory response	↑ Inflammatory response
	↑ Free radical production
	↑ Intracellular acidosis
	Destabilized cytoskeleton

From Hindler K, Nussmeier NA. Central nervous system risk assessment. In: Newman M, Fleisher L, Fink M, eds. *Perioperative Medicine: Managing for Outcome*. Philadelphia: Saunders; 2008:69-88.

mechanisms for the neuroprotective effects of hypothermia have been tested in animal models (Table 54.11).²⁸⁴ Hypothermia may attenuate the effects of cerebral ischemia by creating a favorable balance between oxygen supply and demand, and by decreasing the cerebral metabolic rate of oxygen. Hypothermia not only reduces the metabolic rate but also delays the release of excitatory amino acids, neurotransmitters that play an important role in the process of neuronal death. Additionally, hypothermia reduces the permeability of brain arterioles and prevents blood-brain barrier dysfunction. Hypothermia may also interfere with the inflammatory response by suppressing the adhesion of polymorphonuclear leukocytes in the damaged region.

However, after performing a meta-analysis, Rees and colleagues concluded that no definitive evidence for a neuroprotective effect of hypothermia during routine CPB exists,²⁸⁵ although the studies examined in that analysis had some important limitations. For example, the timing of hypothermia may have limited its protective value. Hypothermia is always initiated after aortic cannulation and the onset of bypass, but macroembolization to the brain is unlikely during this period because the heart is excluded from the circulation by the aortic cross-clamp. Instead, the periods of highest risk for microembolization and macroembolization are during and shortly after aortic manipulation, cross-clamping, and unclamping because aortic cannulation and cross-clamping are performed near the start of CPB, when the brain is not yet cold. Similarly, the aortic cross-clamp is removed near the end of CPB, usually after the patient has been rewarmed.

In contrast, hyperthermia is known to be deleterious. Elevation of body temperature by as little as 2°C decreases cerebral tolerance to ischemia. Hyperthermia delays neuronal metabolic recovery and increases excitotoxic neurotransmitter release, oxygen free radical production, intracellular acidosis, and blood-brain barrier permeability, with subsequent multifocal breakdown at sites in the thalamus, hippocampus, and striatum (see Table 54.11). Hyperthermia also affects protein kinase activity and destabilizes the cytoskeleton. Clinically, fever and hyperthermia worsen the prognosis of hospitalized patients with stroke.²⁸⁶

TABLE 54.12 Summary of Blood Gas Management Strategies

Strategy	Goal	Implementation	Total CO ₂ Content	Theoretic Benefits
α-stat	Achieve electrochemical neutrality by maintaining a constant OH ⁻ /H ⁺ ratio	Use normal <i>temperature-uncorrected</i> blood gas values	Constant	Preserves enzyme function and cerebral autoregulation
pH-stat	Maintain constant pH	Use normal <i>temperature-corrected</i> blood gas values	Increases	Produces more homogeneous brain cooling; decreases brain O ₂ consumption
Combination	Maintain constant pH during cooling, then restore electrochemical neutrality before circulatory arrest	During the cooling phase, use <i>temperature-corrected</i> values, then switch to <i>temperature-uncorrected</i> values before interrupting flow; use <i>temperature-corrected</i> values during the rewarming period	Initially increases during cooling, then returns to baseline	Produces homogeneous brain cooling, then restores neutrality; improves CMRO ₂

CMRO₂, Cerebral metabolic rate of oxygen; CO₂, carbon dioxide; O₂, oxygen; OH⁻/H⁺, ratio of hydroxyl ion to hydrogen ion.

In the 1990s, some centers began using normothermic cardioplegia to improve cardiac outcomes while avoiding deliberate hypothermia. This practice of “warm heart surgery” was debated because of concern that the neuroprotective effects of hypothermia would be lost. Subsequent studies produced inconsistent results with respect to the incidence of stroke and postoperative neurocognitive decline. Such differences in neurologic outcome may have resulted from variations in the temperature management strategies used in different “warm heart surgery” studies; these variations ranged from allowing a downward “drift” that resulted in actual mild hypothermia to active rewarming that may have led to inadvertent cerebral hyperthermia.²⁸⁷

In patients undergoing CPB, cerebral hyperthermia during the rewarming period may aggravate any cerebral injury that has occurred. Aggressive rewarming was once commonly practiced to prevent the “afterdrop” in temperature that usually occurs after CPB is discontinued, but this practice can cause cerebral hyperthermia at the exact moment when cerebral embolization is most likely. Therefore, rewarming should be gradual and should start early enough to achieve stability of the desired temperature before CPB is terminated.²⁸⁸

The surgeon should also be aware of the limitations of any temperature-monitoring site used during CPB. Brain parenchymal temperature cannot be measured directly during cardiac surgery; rather, it must be estimated from tympanic, nasopharyngeal, esophageal, rectal, bladder, skin surface, pulmonary arterial, or jugular venous bulb temperature. However, concordance between cerebral temperature and temperatures measured at most of these sites is poor.^{289,290} Jugular bulb temperature is generally considered to be the gold standard because the proximity of the jugular bulb to the carotid artery origins and the aortic cannula makes jugular bulb temperature more similar to brain temperature than are temperatures measured at other commonly used sites (class I, Level C).^{290,291} Temperatures measured at the nasopharyngeal, esophageal, bladder, rectal, or skin surface sites underestimate jugular bulb temperature during rewarming.^{289,290} Because monitoring jugular bulb temperature is not usually feasible, monitoring the temperature of the blood in the arterial line that exits the oxygenator is considered the closest surrogate for brain temperature.^{290,292} Temperature measured in the PA or the

nasopharynx (class IIa, Level C) are also reasonable sites to monitor during weaning from CPB.

Hyperthermia that develops postoperatively may be just as hazardous as intraoperative hyperthermia. Temperatures exceeding 38.5°C are common during the first 48 hours after cardiac surgery and occur in nearly 40% of patients.²⁹³ This postoperative hyperthermia is known to be correlated with increased cognitive dysfunction 6 weeks after cardiac surgery.²⁹⁴ Therefore, hyperthermia in the postoperative period should be treated with antipyretics and, if necessary, active body surface cooling.

In summary, patients maintained on CPB should be rewarming early and slowly. No monitored temperature should be allowed to exceed 37.0°C.²⁹² This practice prevents cerebral overheating.

Blood Gas Management

Temperature has a significant effect on the solubility of gases in solution. Specifically, in blood gas analysis, the carbon dioxide concentration (and consequently the pH) is profoundly altered by changes in temperature. As temperature decreases, the partial pressure of arterial carbon dioxide (PaCO₂) decreases as carbon dioxide becomes more soluble in plasma. Therefore, inducing hypothermia during CPB poses a dilemma in terms of how best to approach acid-base management at lower temperatures (i.e., whether *temperature-corrected* or *temperature-uncorrected* blood gas values should be used to manage the patient’s care). This question has been the basis for a decades-old debate: α-stat versus pH-stat blood gas management (Table 54.12).

α-Stat Hypothesis. In aqueous systems, neutrality (pN) is said to occur when $[H^+] = [OH^-]$. The dissociation of water depends on temperature; therefore, the pH value at which pN occurs varies with the temperature. Acid-base comparative physiologic studies of animals whose blood temperature varies (i.e., ectotherms and poikilotherms) suggest that blood and intracellular pH values parallel the temperature-related changes seen in the neutrality of water.²⁹⁵ From these findings emerged the α-stat strategy, which endeavors to maintain intracellular electrochemical neutrality across all temperatures.

Maintaining this neutrality requires an appropriate buffering system. It is thought that protein buffering is largely responsible for maintaining this temperature-pH

relationship. Specifically, the imidazole group of the amino acid histidine has a dissociation constant (pK_a) value similar to that of blood. Therefore, if carbon dioxide stores are held constant during cooling, the ionization state (termed α) will remain constant. This may be important because the ionization state affects both the structure and the function of proteins. Keeping the charge state constant (α -stat) by allowing blood pH to change with the neutrality of water is thought to be essential for maintaining the most physiologically beneficial structure and function of enzymes during hypothermia. Research suggests that when the α -stat strategy is used, cerebral autoregulation remains largely intact until deep hypothermic temperatures are reached.²⁹⁶

To manage acid-base balance during hypothermic CPB by using the α -stat approach, one must maintain temperature-uncorrected blood gas values. The term *uncorrected* is often confusing because it refers to the values that the blood gas machine typically reports without being programmed to correct the values to the actual temperature of the patient. For example, blood drawn from a patient undergoing CPB at 18°C is measured in a blood gas machine, which anaerobically warms the sample to 37°C and reports values at normothermia. With α -stat management, one would strive for normal temperature-uncorrected results, which would theoretically maintain intracellular electrochemical neutrality.

pH-Stat Hypothesis. An alternative strategy is the pH-stat approach to acid-base management. The pH-stat strategy endeavors to maintain a constant pH despite changes in temperature. Hibernating animals tend to follow this strategy. To counter the tendency of cooling blood to follow the neutrality of the water curve and become more alkalotic as temperature decreases, these animals increase their blood carbon dioxide content and maintain normal pH at hypothermic body temperatures.

Carbon dioxide is a potent cerebral vasodilator; therefore, the increase in carbon dioxide content during pH-stat management uncouples cerebral autoregulation; cerebral blood flow increases independent of cerebral metabolic demand. These effects are thought to be neuroprotective for infants maintained on CPB who may have aortopulmonary collateral vessels and also to promote deep homogeneous cooling of the brain before circulatory arrest.²⁹⁷ However, during rewarming, the higher cerebral blood flow that results from using pH-stat management may increase the embolic load sent to the brain.

Using the pH-stat strategy with CPB involves managing blood gas parameters with temperature-corrected values by programming the blood gas machine to correct the values to the patient's body temperature. During bypass, decreasing blood temperature increases the solubility of carbon dioxide and, consequently, results in decreased $Paco_2$ values. Therefore, the perfusionist must either decrease the "sweep speed" of the air-oxygen mixture or, less commonly, add carbon dioxide to the oxygenator ventilation system to increase the carbon dioxide content and maintain a $Paco_2$ of 40 mm Hg (and normal pH) as the temperature of the blood decreases. The extracorporeal circuitry must be equipped with an in-line blood gas analyzer so that $Paco_2$ levels can be continually monitored during CPB.

Which Strategy Is Best? In adult patients, several independent, prospective randomized trials have shown that using α -stat management during moderate hypothermia produces better neurologic outcomes than observed with pH-stat management. These and other data have led to an evidence-based recommendation (ACC/AHA class I, level A) that α -stat management be used in adults undergoing moderate hypothermic CPB.^{288,298} It is unclear which strategy is superior in adults when deep hypothermia is used with or without circulatory arrest.

In pediatric CPB, however, several human and animal studies suggest that pH-stat management may be more beneficial than α -stat management for infants. These studies showed that pH-stat management produced more homogeneous cooling, less oxygen consumption, and better cerebral metabolic recovery than did α -stat management. The clear trend in pediatric CPB is to use pH-stat alone or in combination with α -stat (i.e., to use pH-stat during cooling and α -stat during rewarming) when deep hypothermia is used.²⁹⁹

Inflammatory Response to Cardiopulmonary Bypass

Since the 1980s, much has been written about the rapid and profound inflammatory response that CPB elicits. Surgical stress itself causes an inflammatory response, which CPB aggravates by subjecting the patient's blood to contact with foreign surfaces, ischemia and reperfusion, and gaseous and particulate microembolization, which initiate and amplify multiple redundant and interconnected immune cascades. With the onset of CPB, the increased expression of *initiator* substances (including endotoxin, tumor necrosis factor [TNF], and nuclear factor κ B, as well as anaphylatoxins and cytokines) stimulates *effector* cells (including polymorphonuclear neutrophils, platelets, and endothelial cells) to upregulate adhesion molecules and release cytotoxic oxygen radicals and proteases. This response can produce tissue injury of varying degree in a variety of organ systems.

Numerous clinical approaches have been shown to reduce the inflammatory response measurably in cardiac surgical patients (Fig. 54.17). These approaches can be loosely grouped into three primary categories: modification of surgical and perfusion techniques, modification of circuit components, and pharmacologic strategies.

Modification of Surgical Techniques or Perfusion Techniques

Modification of Surgical Technique. The movement toward minimally invasive cardiac surgery is at least partly motivated by the goal of reducing inflammation in the patient. The term *minimally invasive* may refer to procedures that use modified surgical techniques, including miniature incisions with or without robotic assistance, and to procedures that use classic surgical approaches that minimize or eliminate the use of CPB and thus exposure to the ECC (e.g., OPCAB). Although OPCAB does not eliminate the patient's inflammatory response, it may produce less expression of inflammatory cytokines than does CABG with CPB.³⁰⁰ However, it may be that the OPCAB-related reduction in inflammation is minimal in the days after the surgical procedure.³⁰¹ Moreover, any improvements in outcomes that

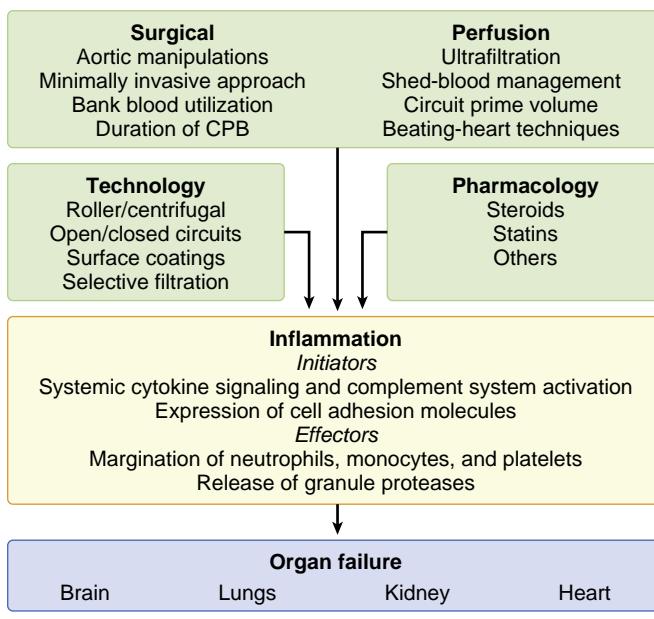


Fig. 54.17 Brief review of the current understanding of the many variables that influence the inflammatory response in patients undergoing cardiopulmonary bypass (CPB).

may be attributable to the use of OPCAB instead of standard CABG are probably not exclusively caused by elimination of the ECC. Rather, minimizing or eliminating aortic manipulation, particularly in patients with severe atherosclerosis, may independently reduce the incidence of stroke.⁴³

Modification of Perfusion Techniques. Reasons for the lack of consensus on the exact contribution of CPB to the inflammatory process include the issue that perfusion practice is far from standardized.²⁹⁸ Various perfusion techniques and technologies have been shown to reduce inflammation, including shed-blood management,³⁰² ultrafiltration,^{303,304} temperature management,²⁸⁵ circuit miniaturization,^{305,306} and on-pump beating-heart techniques.³⁰⁷

Perfusion Technology

In addition to the ways in which perfusion technology is used, the type of technology used may moderate the inflammatory response to CPB. No consensus exists regarding which arterial pump technology—roller pumps or centrifugal pumps—is less hemolytic. Some investigators have shown that using modified surface materials in the CPB circuit, such as heparin coatings, may reduce inflammation.³⁰⁸⁻³¹⁰ Additionally, selective filtration of leukocytes with an in-line leukocyte filter has been proposed as a method for reducing the concentration of activated leukocytes and inflammation. Warren and associates,³¹¹ in a review of 63 studies, concluded that leukocyte filtration may have some modest benefits, but definitive evidence of any improvement in inflammatory-mediated complications is insufficient. Additionally, hemoconcentrators may be able to remove inflammatory mediators from circulation through large-volume zero-balance ultrafiltration techniques,³⁰⁴ but little evidence exists of significant clinical improvements in the adult CPB population.

Pharmacologic Strategies

After decades of laboratory studies and clinical trials, a rigorously vetted pharmacologic approach to reducing inflammation in CPB-supported patients is still lacking. The best-established drug, aprotinin, was removed from the market in 2007 because of concerns about an increased risk of acute kidney failure after administration.¹¹⁹ Thus, the clinician is left to select from a short list of drugs whose use is supported only by mixed mechanistic results and insipid evidence of improved clinical outcomes.

Corticosteroids have been used in cardiac surgery for decades for their immunosuppressive and antiinflammatory effects. The results of meta-analyses of small randomized clinical trials of methylprednisolone or dexamethasone have yielded conflicting results.^{312,313} These drugs may reduce the incidence of atrial fibrillation, but they may also increase gastrointestinal bleeding, and they did not influence postoperative mortality or cardiac or pulmonary complications.^{312,313} The first large (4494 patients) randomized controlled clinical trial of the use of routine corticosteroids during cardiac surgery in adults showed that high-dose (1 mg/kg) dexamethasone did not reduce the 30-day incidence of major adverse events (death, MI, stroke, renal failure, or respiratory failure).³¹⁴

One meta-analysis of randomized controlled studies of the use of prophylactic preoperative statins to reduce inflammatory mediators concluded that evidence indicates that statins reduce plasma concentrations of IL-6, IL-8, TNF- α , and CRP when doses of 20 to 80 mg/day are administered for 1 day to 3 weeks preoperatively.³¹⁵ In a Cochrane Database review of 11 randomized controlled trials performed in patients undergoing on- or off-pump cardiac surgical procedures, pooled analysis showed that statin pretreatment before surgery reduced the incidence of postoperative atrial fibrillation and was associated with a shorter length of stay in the ICU but failed to influence mortality.³¹⁶ Finally, a meta-analysis of 14 studies of ketamine, which may also have antiinflammatory effects, suggests that ketamine administration significantly reduces the IL-6 response to surgery.³¹⁷

DEEP HYPOTHERMIC CIRCULATORY ARREST

DHCA involves reducing the patient's core temperature to profoundly hypothermic levels (15°C-22°C) before globally interrupting blood flow to the body, draining all the blood out of the patient, and collecting it in the ECC reservoir. In adults, this procedure is primarily used during surgical repair of the aorta, especially in cases of dissection or aneurysm involving the transverse arch.

Deliberate hypothermia with systemic cooling is the only reliable method of neuroprotection during complete global ischemia. Some clinicians also put ice bags on the patient's head to augment or maintain cerebral cooling. Pharmacologic approaches to neuroprotection, such as administering steroids to reduce inflammation or barbiturates or propofol to induce burst suppression, are used in some centers, although evidence to support their efficacy in the setting of complete global ischemia is scant. Furthermore, if the EEG is monitored, it is important to induce EEG isoelectricity with hypothermia before commencing the period of circulatory arrest rather than relying on supplemental barbiturates or propofol to provide neuroprotection.³¹⁸

The equipment and circuitry of the heart and lung machine used for DHCA procedures are not generally different from those used for standard CPB procedures. Blood gas management during cooling and rewarming for DHCA procedures typically follows the α -stat management scheme in adult patients and the pH-stat management scheme in pediatric patients (see the earlier section on blood gas management). Systemic cooling is begun when CPB is initiated and is continued until the temperature of the patient is low enough to provide adequate protection for the anticipated duration of circulatory arrest. When deciding what temperature is “adequate,” one must give top priority to protecting the brain. Because no clinically feasible method for measuring brain temperature is available, surrogate temperatures must be used to estimate core temperature (see the earlier section on temperature). A time lag exists between the time that arterial blood reaches a target temperature and the time that the brain’s parenchymal tissue equilibrates with the blood temperature. Consequently, when aggressive cooling is used, arterial blood temperature underestimates brain temperature. For an average-sized adult, cold arterial perfusion at full CO flow should be continued for 20 to 30 minutes after the “goal” arterial blood temperature is reached to ensure that the brain has had sufficient time to cool. For an anticipated circulatory arrest period of 30 to 40 minutes, a temperature of 18°C to 20°C is probably adequate; however, slightly warmer temperatures may be acceptable if a shorter period of arrest is used or if cerebral perfusion is maintained.³¹⁹ It is also good practice to monitor temperatures at multiple sites on the patient, in addition to blood temperature, to observe the relative change over time during cooling and rewarming. Furthermore, the EEG provides a good pharmacodynamic endpoint for the cerebral effects of cooling; hypothermia-induced EEG isoelectricity should be present before elective circulatory arrest commences.³¹⁹

As the patient cools, the viscosity of blood will increase. At a temperature of 18°C, the viscosity of blood with a hematocrit of 30% to 35% increases to three to four times its normal level. Cardiac surgical textbooks suggest that hemodilution is important in minimizing any microcirculatory disturbances that may occur because of increased blood viscosity. Consequently, some clinicians may target a hematocrit value that is appropriate to the patient’s temperature during DHCA, approximately 18% to 20%. However, the results of a study performed in piglets by Duebener and colleagues suggested that a hematocrit of 30% is preferable if DHCA is used.³²⁰

When the patient has reached an appropriate core temperature as determined by temperatures measured at multiple sites and after adequate time for equilibration, the arterial blood flow from the pump is stopped, and the patient’s blood is drained into the ECC reservoir. During the period of circulatory arrest, the blood in the ECC reservoir should be recirculated to prevent stasis and maintain the desired temperature. Gas flow to the oxygenator should be discontinued to prevent profound hypocapnia. Reperfusion should be initiated with cold blood. An initial period (5–10 minutes) of cold reperfusion may enhance cerebral protection by removing accumulated metabolic products from the cerebral capillary beds while maintaining a low cerebral metabolic rate of oxygen.

The risk of neurologic injury after cardiac surgery involving DHCA extends into the postoperative period because cerebral vascular resistance is increased and cerebral blood flow is decreased for several hours after the procedure. In addition, hyperthermia, possibly secondary to a systemic inflammatory response, is common in the postoperative period and should be treated aggressively.

In an effort to reduce the period of cerebral ischemia during circulatory arrest, selective cerebral perfusion techniques have been developed. Selective antegrade cerebral perfusion can be accomplished by directly cannulating the left common carotid artery,³²¹ or perfusion can easily be delivered through the right common carotid artery when the aortic cannulation approach for CPB involves cannulating the axillary or innominate artery.³²² Axillary cannulation facilitates the delivery of arterial blood from the ECC to the entire circulatory system during cooling and rewarming or, with the addition of a clamp to the proximal innominate artery, selectively into the right common carotid and radial arteries. Because of the proximity of the arterial cannula to the right radial artery, arterial blood pressure monitored in the right radial artery may be significantly higher than pressure monitored in the left radial or femoral artery. Consequently, right radial arterial pressure should not be used to control perfusion during cooling and rewarming. During delivery of selective antegrade cerebral perfusion, cold arterial blood from the extracorporeal circuit should be delivered to maintain the cerebral blood pressure between 30 and 60 mm Hg. The perfusion flow rates necessary to achieve this pressure vary depending on the site or sites of arterial cannulation. Direct cannulation of only the left common carotid artery requires the least flow, whereas cannulation of multiple head vessels or of the axillary artery (which perfuses the right common carotid, right internal thoracic artery, and right arm) requires higher flow rates. Subsequently, flow rates of 150 to 1500 mL/min have been reported. Selective retrograde cerebral perfusion is delivered through a snared cannula introduced into the right atrium and advanced into the SVC; this type of perfusion can be initiated after the patient’s systemic perfusion is discontinued. Cold oxygenated blood from the ECC can be administered at a flow rate (\approx 5 mL/kg/min) high enough to maintain SVC pressure between 35 and 40 mm Hg.³²³ Although some debate remains about whether selective cerebral perfusion of any kind is necessary to achieve optimal neurologic outcome after DHCA procedures,³²⁴ investigators generally agree that antegrade cerebral perfusion, when used properly, is superior to retrograde perfusion.^{325,326}

LEFT HEART BYPASS

If a descending aortic aneurysm or aortic dissection is to be surgically replaced with a tube graft, blood flow through the patient’s thoracic aorta must be interrupted. The application of vascular clamps to this major vessel acutely increases the afterload of the heart and produces global ischemia in all parts of the body distal to the clamp. Patients with compromised cardiac function or those undergoing a surgical procedure in which the duration of ischemia will be unacceptably long require some method of circulatory support. Temporary interposition of a shunt (e.g., a Gott shunt) around the area of repair is the simplest approach, but it does not offer the level of support that can be achieved with LHB or CPB.

For these procedures, the approach is usually through a left thoracotomy incision, which provides excellent access to the left atrium. The simplest approach to LHB is to withdraw blood from the left atrium with a centrifugal pump and return the blood to the patient's femoral artery. This *simple* LHB circuit gives the clinician excellent control of blood flow distal to the clamps and therefore the ability to manipulate the afterload against which the heart must work. However, the complexity of some surgical procedures requires that full CPB be used.

Surgical complications are not uncommon in these patients and include hypoxia, hypothermia, and exsanguination. A double-lumen endotracheal tube or bronchial blocker is often used to isolate the left lung from the right. After left thoracotomy and exposure of the aneurysm, ventilation of the left lung is discontinued. Patients with preexisting lung dysfunction or traumatic lung injury associated with aortic dissection may have difficulty maintaining oxygenation with a single lung. Because of the large surgical exposure required and the sometimes extended duration of the procedure, it is not unusual for the patient to become hypothermic. Furthermore, these procedures carry an elevated risk of blood loss and the consequent need for rapid replacement of fluids and blood products. It is often advisable to use *complete* LHB to reduce these risks. Currently the

use of LHB has decreased in clinical practice because of the widespread application of endovascular techniques for the treatment of descending aorta pathologies.

Fig. 54.18 illustrates the simple-circuit and complete-circuit approaches to LHB. The major difference between a complete LHB circuit and the standard CPB circuit is the position of the reservoir in the circuit and the position of the venous cannula in the patient. In a complete LHB circuit, the reservoir does not receive the blood returning from the patient as in the CPB circuit. With the reservoir out of the pathway of the blood, the effective surface area of the ECC is reduced; this reduction attenuates contact activation of the blood and minimizes the need for high-dose heparinization.

In both circuits, the management goal is the same—to keep arterial blood pressure higher than 60 mm Hg both proximal and distal to the aortic cross-clamp throughout the procedure. However, the complete LHB circuit gives the clinician the ability to manage hypoxia, hypothermia, and blood loss. The addition of an oxygenator to the circuit makes it possible to augment the patient's ventilation and oxygenation. The heat exchanger is used to maintain normothermia. The reservoir facilitates the addition of large volumes of fluid or blood products in the event of hemorrhage, hypovolemia, or both.

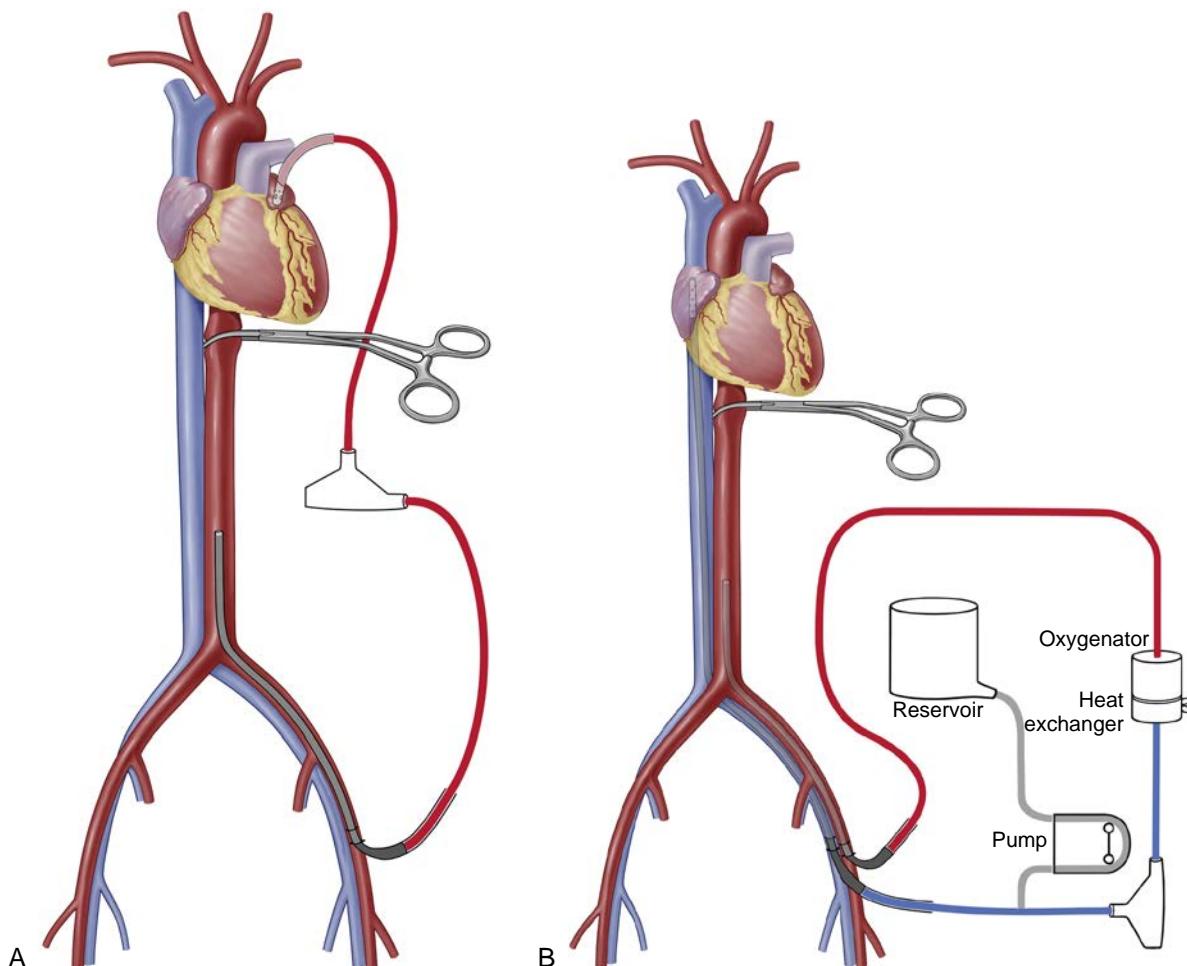


Fig. 54.18 Left heart bypass (LHB) diagram. (A) Simple LHB (left atrium, cone, and femoral artery). (B) Complex LHB (including an oxygenator, heat exchanger, and reservoir for fluid administration).

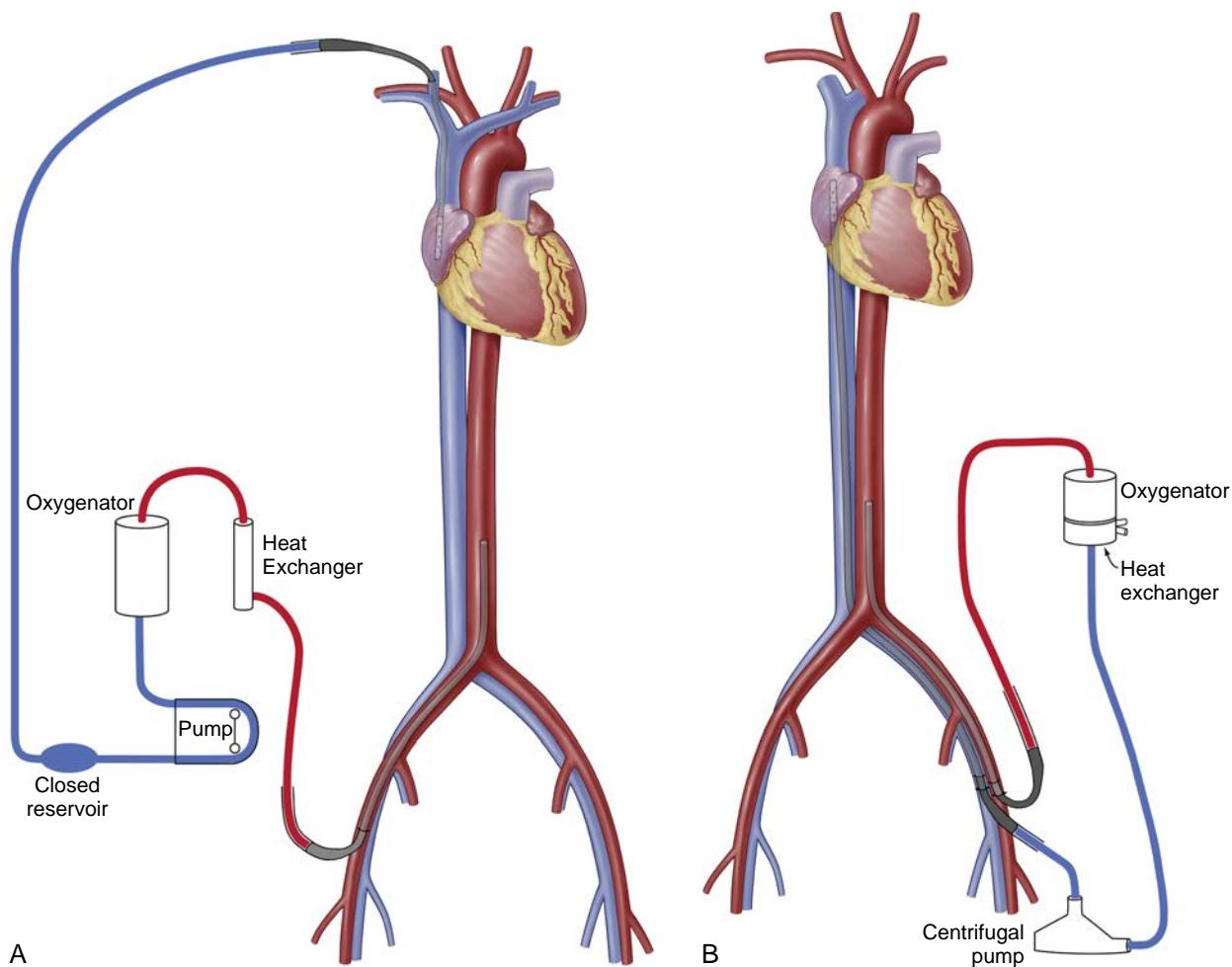


Fig. 54.19 (A) Patient cannulated through the internal jugular vein and femoral artery, with a traditional extracorporeal membrane oxygenation circuit. (B) Patient cannulated through the femoral vein and femoral artery, with a simple cardiopulmonary support circuit.

CARDIOPULMONARY SUPPORT AND EXTRACORPOREAL MEMBRANE OXYGENATION CIRCUITS

For all practical purposes, no difference exists between a CPS circuit and an ECMO circuit. Both consist of a CPB circuit without a reservoir, an arterial line filter, or any of the ancillary pumps that are used during cardiac surgery (i.e., pump suction, vent, and cardioplegia). Because the reservoir is removed from the circuit, these systems are considered closed. Closed circuits have a static internal volume and cannot unload the patient's vascular system.

The removal of the reservoir and filters from the circuit has advantages and disadvantages. The chief advantage is that the surface area of the circuit is significantly reduced, which facilitates a reduced anticoagulation regimen with an initial heparin dose of 75 to 150 units/kg and a continuous infusion of heparin at 25 to 75 units/kg/h to maintain ACTs of 180 to 250 seconds.[†]

The chief disadvantage is that the closed circuits are less able to trap emboli. Special precautions should be taken

when connecting a closed ECC to the patient's cannulas, injecting fluids and medications into the circuit, or sampling from the venous line. Additionally, because of the reduced anticoagulation regimen, blood stasis in the circuit should be avoided, and periods of low flow should be minimized.

In intensive care settings, ECMO or CPS is used to support the heart, lungs, or both for days or weeks. The newer generation of centrifugal pumps and hollow-fiber oxygenators perform acceptably well during these long-term applications and are becoming more commonly used in desperate situations (Fig. 54.19).

Specific Cardiovascular Disease States

CORONARY ARTERY DISEASE

Pathophysiology of Coronary Disease

Coronary Anatomy. Understanding the coronary anatomy is important to understand the pathophysiology of CAD and the anesthetic care of patients undergoing myocardial revascularization. Two main coronary arteries take off from the aorta and supply the myocardium: the left main coronary

[†]For Extracorporeal Life Support Organization (ELSO) anticoagulation guidelines see <https://www.elso.org/Portals/0/Files/elsoanticoagulationguideline8-2014-table-contents.pdf>

artery (LMCA) and the RCA. The LMCA subsequently divides into the left anterior descending (LAD) coronary artery and the left circumflex artery (LCx). The LAD courses down the interventricular groove and gives rise to the diagonal and septal branches. The diagonal branches of the LAD supply the anterolateral aspect of the heart. The septal branches supply the interventricular septum, as well as the bundle branches and the Purkinje system. The LAD itself terminates at the apex of the LV. The other branch of the LMCA, the LCx, courses along the left AV groove and gives rise to one to three obtuse marginal branches that supply the lateral wall of the LV. In 45% of patients, the sinus node arterial supply arises from the LCx. In 15% of patients, the LCx gives rise to the posterior descending artery, which supplies the posterior inferior aspect of the LV ("left-dominant" system).

The RCA traverses the right AV groove and supplies the right anterior wall of the right ventricle through its acute marginal branches. In 85% of the population, the RCA gives rise to the posterior descending artery supplying the posterior inferior aspect of the LV ("right-dominant" system). The AV node arterial branch arises from the dominant artery to supply the node, the bundle of His, and the proximal part of the bundle branches. In addition, in 55% of the population, the sinus node arterial supply arises from the RCA.

Determinants of Myocardial Oxygen Supply and Demand. The balance of oxygen supply versus demand is somewhat complex (Figs. 54.20 and 54.21). Oxygen supply is determined by the oxygen content of arterial blood and by coronary blood flow. Extraction of oxygen from

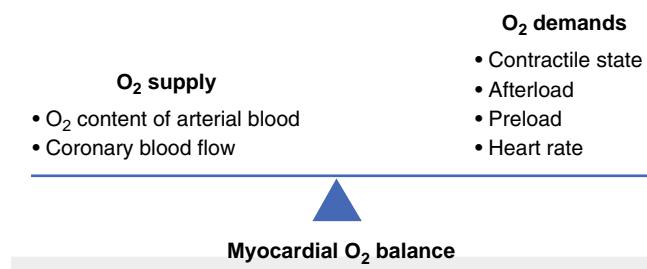


Fig. 54.20 Factors determining myocardial oxygen (O₂) supply and demand. (From Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:524.)

arterial blood is maximal at rest. As demand increases (with exercise or hemodynamic stress), the oxygen supply to the myocardium must also increase.

Determinants of blood flow in normal coronary arteries include the pressure differential across the coronary bed (i.e., the coronary perfusion pressure) and coronary vascular resistance. The coronary perfusion pressure for the LV is the aortic blood pressure during diastole minus the LV end-diastolic pressure (LVEDP); thus, elevations in LVEDP impede subendocardial blood flow. Because coronary stenosis causes vessels to dilate maximally distal to the stenosis, manipulating coronary perfusion pressure is an important means of controlling coronary blood flow (and preventing or treating myocardial ischemia). However, because the determinants of myocardial oxygen balance interact in a complex manner, altering any one of them can have multiple effects. For example, a rise in blood pressure increases coronary blood flow but also increases afterload, thereby elevating wall tension and oxygen demand.

The duration of diastole is another important factor affecting oxygen supply to the myocardium because 70% to 80% of coronary arterial blood flow occurs during the diastolic phase of the cardiac cycle. During the systolic phase, cardiac contraction increases intraventricular cavity pressure and coronary vascular resistance, thus impeding myocardial perfusion. The total time per minute spent in diastole is a function of the heart rate, but a nonlinear relationship exists between heart rate and the duration of diastole (Fig. 54.22). This is a major reason for the use of β -blockers as antiischemic drugs, both for long-term therapy and for preventing even small increases in heart rate during the perioperative period.

The oxygen content of blood depends on hemoglobin-bound oxygen and, to a lesser extent, dissolved oxygen. Although a high hemoglobin level gives the blood high oxygen-carrying capacity, the minimum level of hemoglobin necessary to avoid ischemia has not been well defined in clinical studies. Factors that affect this limit include the severity of CAD, the heart rate, perfusion pressure, and myocardial wall thickness and tension. Furthermore, delivery of oxygen to myocardial tissue also depends on a high partial pressure of oxygen (PO₂), and actual release of oxygen from hemoglobin occurs according to the oxyhemoglobin

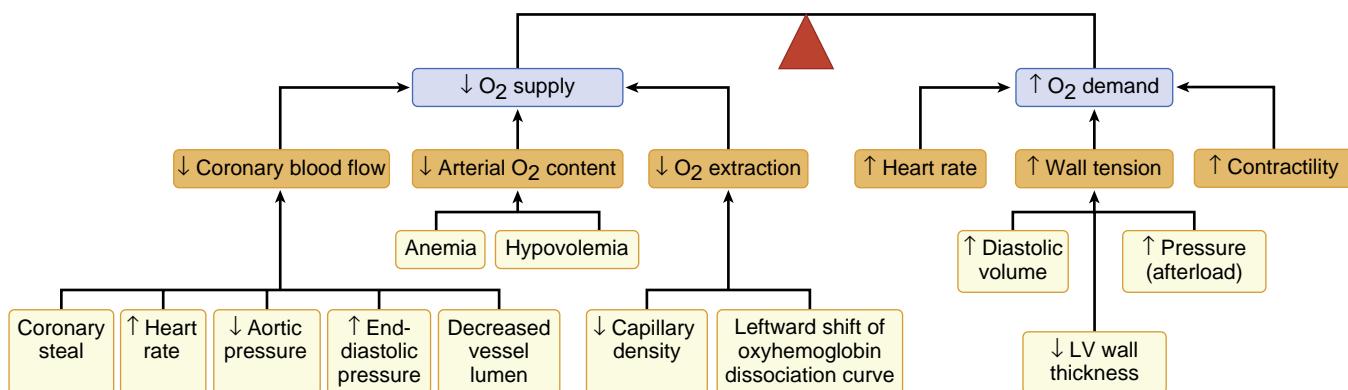


Fig. 54.21 Summary of factors that affect myocardial oxygen supply and demand. LV, Left ventricular. (From Green MS, Okum GS, Horow JC. Anesthetic management of myocardial revascularization. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:319–358; and Modified from Crystal GJ. Cardiovascular physiology. In: Miller RD, ed. *Atlas of Anesthesia*, Vol 8, *Cardiothoracic Anesthesia*. Philadelphia: Churchill Livingstone; 1999:1.)

dissociation curve. A leftward shift of this curve caused by alkalosis, hypothermia, or low levels of 2,3-diphosphoglycerate decreases the release of oxygen.

In patients undergoing myocardial revascularization, reductions in myocardial oxygen supply may occur because of hypotension, tachycardia, anemia, or coronary vasoconstriction, as well as increases in demand secondary to tachycardia or increased afterload. Although myocardial ischemia is certainly possible without any changes in systemic hemodynamics, vigilant monitoring for imbalances in myocardial oxygen supply versus demand, as well as monitoring for the development of ischemia, is necessary throughout the perioperative period. Myocardial ischemia may be detected by ECG monitoring and ST-segment analysis, as well as by TEE monitoring for the development of regional wall motion abnormalities.

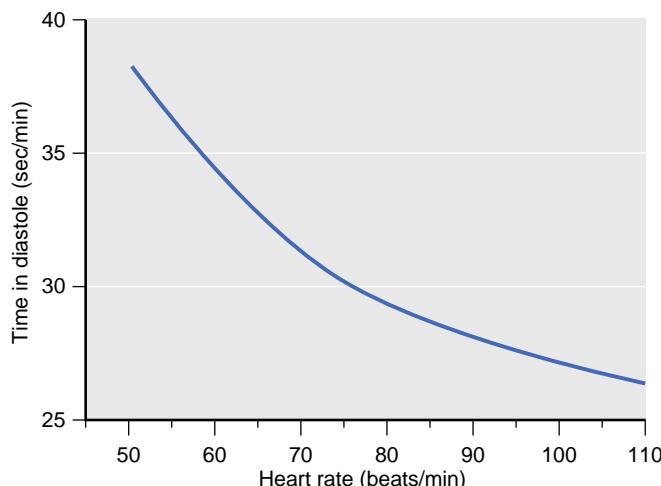


Fig. 54.22 Total time spent in diastole each minute plotted as a function of heart rate in beats per minute. The reduction in diastolic interval leads to diminished left ventricular blood flow as heart rate increases. (From Green MS, Okum GS, Horrow JC. Anesthetic management of myocardial revascularization. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:298.)

On-Pump Coronary Artery Bypass Grafting Surgery

Preoperative Evaluation. Typically, patients undergoing CABG have had extensive preoperative assessment of their cardiac disease (see [Chapter 31](#)). Coronary artery anatomy should be noted, particularly a high-grade lesion in the LMCA or proximal LAD coronary artery or triple-vessel disease. Ventricular function, assessed by angiography or echocardiography, is usually recorded as an estimated EF. Other cardiac disease discovered in the preoperative workup should be noted and understood, including valvular abnormalities such as concurrent MR, aortic stenosis (AS), aortic insufficiency, atrial septal defect (ASD) or ventricular septal defect (VSD), or ventricular aneurysm. The anesthesiologist should be aware of any abnormal cardiac rhythm on the ECG or noted in the history, such as atrial fibrillation or other supraventricular tachycardia (which may lead to hemodynamic instability or increase the patient's risk of an embolic neurologic complication), left bundle branch block or a prolonged PR interval (which may progress to a more advanced heart block), or complete heart block, which may be underlying a paced rhythm. Antiarrhythmic therapy, with either pharmacologic drugs or devices such as a pacemaker or automated implantable cardioverter-defibrillator (ICD), should be noted.

Various models for assessing overall risk have been developed that include certain factors associated with increased risk: poor LV function (history of CHF or LVEF <30%), advanced age, obesity, emergency surgery, combined procedures (e.g., valve repair or replacement combined with CABG), prior cardiac surgery, and history of diabetes or renal failure ([Table 54.13](#)).^{327,328}

Premedication. In the current era, cardiac surgical patients often have same-day admissions. Frequently, the only premedication they receive is midazolam on the morning of the surgical procedure, to allay anxiety. However, small additional doses of midazolam, fentanyl, or both may be administered during line placement, especially if the central line is placed before the induction of general anesthesia (see the section on induction of anesthesia and the

TABLE 54.13 Risk Factors Used in Various Risk-Stratification Schemas for Coronary Artery Bypass Graft Surgery

	Montreal	Cleveland	Newark	New York	Northern New England	Society of Thoracic Surgery
Emergency	+	+	+	+	+	+
Poor LV function or congestive heart failure	+	+	+	+	+	+
Redo operation	+	+	+	+	+	+
Gender or small size	-	+	+	+	+	+
Valve disease	-	+	+	+	-	-
Advanced age	+	+	+	+	+	+
Renal disease	-	+	+	+	+	-
Obesity	+	-	+	-	-	-

LV, Left ventricular.

Modified from Green MS, Okum GS, Horrow JC. Anesthetic management of myocardial revascularization. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:293–318.

prebypass period); this may be particularly important in patients with CAD, to minimize undesirable sympathetic stimulation that could cause tachycardia and hypertension. However, administration of these drugs should be incremental and judicious in patients with low CO or significant pulmonary hypertension.

Induction and maintenance of anesthesia. No single anesthetic agent or combination of anesthetic drugs is suitable for anesthetic induction and maintenance in every patient undergoing CABG surgery. Induction of anesthesia for coronary revascularization is often achieved by administering a benzodiazepine (typically midazolam) in combination with a narcotic, usually fentanyl, and a muscle relaxant.³²⁸ However, either etomidate or propofol in combination with a narcotic has frequently been used. The goal is to avoid wide swings in hemodynamics with induction and with subsequent intubation. Typically, volatile agents are used throughout the prebypass, bypass, and postbypass periods. In addition, the volatile anesthetics have several cardioprotective effects, including triggering the preconditioning cascade and mitigating reperfusion injury.¹⁴⁶ Additional midazolam may be given to ensure that intraoperative awareness is avoided.

One factor in the choice of specific anesthetic agents and doses is the patient's preexisting LV function. Patients with normal LV function can have a significant sympathetic response to surgical stimulation that results in hypertension and tachycardia. Use of β -blockers, additional propofol, higher doses of a volatile anesthetic agent, or vasodilators may be warranted if this situation develops. Conversely, in patients with poor LV function, hypotension may develop with the administration of anesthetic agents because of a reduction in CO or vasodilation, or both. Such patients may require vasopressor or inotropic pharmacologic support, or both.

Another factor in the choice of anesthetic agent is the possibility of early extubation within 4 to 6 hours of arrival in the ICU (so-called fast tracking). Patients who have good preexisting cardiac function and who will be undergoing CABG as an isolated procedure are usually candidates for fast tracking. This strategy necessitates the use of agents in dosages that would not keep the patient sedated or render the patient unable to ventilate adequately for a prolonged period. Early extubation may not be appropriate in patients with poor cardiac function, severe pulmonary disease, or obesity or in those undergoing emergency procedures, CABG combined with other procedures, or redo operations.

Monitoring. Monitoring for patients scheduled to undergo coronary revascularization surgery has evolved since the 1960s, in an effort to detect intraoperative ischemia. The standard American Society of Anesthesiologists (ASA) monitors and invasive arterial blood pressure monitoring (with noninvasive blood pressure backup) are always used. Typically, both leads II and V₅ are used for continuous monitoring, as well as automated ST-segment analysis to improve the chances of detecting ischemia.³²⁹

PA catheters are used less commonly now than in the past because several studies have shown that using such catheters does not improve outcome.³³⁰ In fact, the risks inherent in the use of these catheters may actually exceed the benefits.²⁴ Certainly, the absolute PAP is not diagnostic

of ischemia, although waveform changes may be more predictive. For example, the appearance of a new V wave on the PCWP tracing indicates ischemic papillary muscle dysfunction. In addition, specialized PA catheters allow derivation of several indices of cardiac function, including CO, cardiac index, and S_VO₂. Furthermore, some clinicians believe that the PA catheter is useful in the postoperative period when TEE is not available for continuous monitoring of the patient. In summary, use of the PA catheter for routine CABG surgeries has devolved over the years due to risks inherent in misuse of the information that the catheter provides. Practitioners in individual institutions have developed preferences and policies regarding the use of PA catheters in cardiac surgery. Use of the PA catheter mandates that a risk-benefit assessment be made for each individual patient when placing these catheters.

Regional wall motion abnormalities detected by TEE are more sensitive to ischemia than ECG changes or PA catheter waveform and pressure changes.³²⁹ TEE can be used to interrogate regions of the heart representative of all three major coronary arteries simultaneously. This technology is commonly used throughout revascularization procedures to assess regional wall motion by qualitative inspection of radial shortening and wall thickening, and it is particularly useful after revascularization. In addition, TEE is used to assess ventricular preload and contractility, diagnose any valvular abnormalities, evaluate calcific and atherosclerotic lesions at the aortic cannulation sites, and detect LV thrombus and uncommon congenital abnormalities (e.g., ASD or VSD, persistent left SVC). See Chapter 37 for details on the perioperative use of TEE.

Surgical Considerations. Conventional (on-pump) CABG is the most commonly performed procedure in cardiac surgery. A full median sternotomy performed with a sternal saw is standard. Ventilation of the lungs is halted briefly during sawing of the sternum to avoid a pleural tear. An oscillating saw may be used in patients with a previous sternotomy (redo). The risks posed by redo sternotomy include perforation of the right ventricle, damage to existing vein grafts, and ventricular fibrillation from the transmission of electrocautery energy through preexisting sternal wires. Therefore, PRBCs (2 units) should be immediately available, and external defibrillation pads should be positioned before preparation and draping. Furthermore, surgical manipulation of previous vein grafts may result in embolization of atheroma and resultant ischemia. If a complication does occur during sternotomy or exposure of the heart and cannulation sites, emergency bypass may be established by cannulating a femoral artery and vein.

If an IMA is to be used, the surgical table is elevated and often rotated somewhat to the left to facilitate surgical comfort in performing the dissection. Tidal volumes are also reduced to facilitate exposure. Heparin administration usually occurs before the IMA pedicle is clamped, and papaverine may be injected into this vessel. The prebypass period for on-pump CABG may be relatively short (<1 hour) or may require several hours for dissection of the left IMA, right IMA, radial arteries, or any combination of these vessels. In addition, for most CABG procedures, adequate venous conduits must be harvested, and endoscopic saphenectomy is now common.

Before aortic cannulation, TEE or epiaortic echocardiography, or both, provides critical information regarding the presence and precise location of calcification or mobile atherosmas in the aortic arch. The surgeon may request TEE guidance for placement of the retrograde catheter into the coronary sinus; furthermore, if a persistent left SVC is diagnosed, this abnormality may render retrograde cardioplegia problematic.³²⁸ After CPB is initiated, TEE may also be used to ensure correct placement of the LV vent, as well as to verify the absence of LV thrombus in patients with a recent anterior wall MI or aneurysm.

Surgical and technical complications of CABG surgery that manifest as ischemia include (1) poor-quality proximal or distal anastomoses of the grafts, (2) inadvertent incision of the coronary back wall leading to coronary dissection, (3) suturing of the coronary artery closed, (4) inadequate vein graft length resulting in stretching of the vein when the heart is filled, (5) excessive vein graft length leading to kinking of the vein, and (6) vein graft thrombosis.³²⁷ CPB may need to be reinstated to correct surgical causes of ischemia after revascularization. Heparin should be immediately available if emergency reinstitution of CPB becomes necessary.

After bypass, other causes of ischemia include (1) incomplete revascularization resulting from ungraftable vessels or diffuse distal disease, (2) coronary embolization of air or atheromatous debris, (3) coronary spasm, (4) mechanical factors such as vein graft stretching or occlusion of IMA flow secondary to overinflation of the lungs, and (5) thrombus formation.³²⁷ The treatment of ischemia includes administering various drugs: nitroglycerin or vasopressors when SVR is either high or low; nitroglycerin, a calcium channel blocker (diltiazem, nifedipine, or nicardipine), or both to treat coronary spasm; a vasoconstrictor (usually phenylephrine) to “push” intracoronary air through the vasculature when air embolism is suspected; a β -blocker (usually esmolol) to treat tachycardia; and one or more inotropic agents to increase CO if necessary. In addition, AV sequential pacing may be used to improve rate, rhythm, and hemodynamic stability when appropriate. At times, mechanical support with intraaortic balloon counterpulsation or an LV and/or RV assist device (LAVD or RVAD) may become necessary. Residual effects of cardioplegia, a ventricular aneurysm, or pericarditis may cause ST-segment elevation without actual ischemia.

Off-Pump Coronary Artery Bypass Surgery, Minimally Invasive Coronary Artery Bypass Surgery, and Hybrid Coronary Revascularization

Off-Pump Coronary Artery Bypass Surgery. Awareness of the deleterious effects of CPB has driven advocacy for alternative myocardial revascularization techniques, particularly OPCAB surgery. Proponents of OPCAB cite the low morbidity and mortality of patients who undergo this procedure, as well as faster recovery and reduced procedural costs. Data from the STS suggest that approximately 22% of coronary revascularization procedures are being performed off pump.³³¹

The midline sternotomy is the traditional approach used for OPCAB procedures. Potential sources of bypass grafts include the right and left mammary arteries, the saphenous veins, and the radial arteries. The pericardium is incised,

reflected, and secured to the edges of the mediastinum. Special sternal retractors allow the placement of adjustable and flexible fixation devices that work by direct surface pressure on the myocardium, by suction, or by both methods. These devices stabilize the target vessel and allow the surgeon to “verticalize” the cardiac apex out of the pericardial well to access the posteriorly and laterally located vessels (Fig. 54.23). Dosing of heparin for OPCAB cases is institution specific; both full-dose and low-dose regimens are currently in use.

When the target vessel and surrounding myocardium are stabilized, an elastic ligature is placed circumferentially around the coronary artery to minimize bleeding as an arteriotomy is performed. Surgical visualization is also optimized by the application of a blower or mister, held by a surgical assistant, that releases sterile irrigation fluid aerosolized in carbon dioxide gas. Under these conditions, one or more distal coronary anastomoses are performed. The proximal connections of saphenous vein grafts or free arterial conduits are anastomosed directly to the aorta with a side-biting clamp. Alternatively, an indirect proximal connection is made by creating a T-graft (end-to-side anastomosis) to a mammary artery that is still connected to a vascular pedicle on the subclavian artery.

Surgical considerations include (1) obtaining adequate exposure of the anastomosis site, (2) restraining cardiac motion during anastomosis, and (3) preserving myocardium during coronary flow interruption.³³² To achieve the first two goals, the surgeon must use maneuvers that may significantly compromise hemodynamics by several mechanisms, including impairment of biventricular filling, particularly in the thin-walled, easily compressed right ventricle. In addition, altered ventricular filling can result from verticalization of the cardiac ventricular apex (which may kink or partially obstruct venous return) (see Fig. 54.23). Furthermore, myocardial ischemia occurs in native coronary arteries and is exacerbated by temporary elastic suture ligation of a target vessel.³²⁸ Ischemia of distal myocardial segments can occur during anastomosis of bypass grafts, and the degree of functional deterioration depends on the severity of the stenosis and the extent of collateralization.³³²

Therefore, the anesthesiologist must take measures to prevent severe hypotension to minimize the reduction in coronary perfusion caused by these hemodynamic changes and intraoperative myocardial ischemia. Typically, intravascular volume loading (either crystalloid or colloid) and a head-down position of the patient are used, and it is also common to administer a vasoconstrictor drug (either phenylephrine or norepinephrine). When increased mitral insufficiency further exacerbates the hemodynamic changes, repositioning the heart is a simple maneuver that may increase ventricular filling and normalize ventriculoannular geometry.

Monitoring of the patient includes a five-lead ECG and an invasive arterial pressure catheter. PAP and CO measurements or continuous pulse contour CO can be considered.³³² TEE is beneficial, but views are limited during certain portions of the surgical procedure; verticalization of the heart and the application of external compression footplates cause suboptimal imaging. The midesophageal

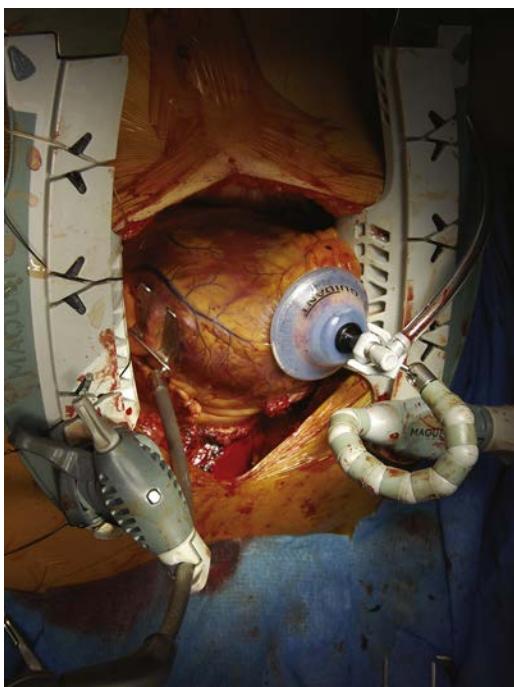


Fig. 54.23 Image depicting the first obtuse marginal (OM1) anastomosis during off-pump coronary artery bypass grafting with a saphenous vein graft. The view is from the head of the patient. The previously completed left internal mammary artery-to-left anterior descending coronary artery anastomosis is seen. The Maquet access device (MAQUET, Wayne, NJ) uses suction to position the heart (verticalization) for easy access to the circumflex coronary artery system. (Courtesy Alexander Mittnacht, MD, Mount Sinai School of Medicine, New York; From Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. St. Louis: Saunders; 2011:524.)

imaging view, rather than the transgastric view, may be best for continuous TEE monitoring while distal coronary anastomoses are performed.

Persistent or worsening ECG change or impending cardiovascular collapse warrants quick action on the part of the anesthesiologist and surgeon. One option is to have a low threshold for the insertion of small, flexible intracoronary stents into the open coronary anastomosis to allow some distal segment flow. Instituting full or partial CPB and placing an IABP are other therapeutic options. Emergency conversion from OPCAB to CABG with CPB, which occurs in approximately 3% of these cases,^{333,334} is not an innocuous event. Such unplanned conversions are reportedly associated with an elevated risk of death, stroke, renal failure, wound infections, and respiratory failure.

The short-term outcomes and long-term efficacy of OPCAB surgery continue to be investigated and debated in the literature. Meta-analyses have noted no significant differences in 30-day mortality.^{335,336} In the largest multicenter randomized trial to compare on-pump CABG with OPCAB, no difference was seen in 30-day mortality or the composite outcome of death and complications.³³⁷ In contrast, very large observational analyses do suggest a mortality benefit. Hannan and associates found a mortality benefit in 49,830 patients from the New York State registry by using a risk-adjusted analysis (i.e., Cox proportional hazard models and propensity analysis).³³⁸ However, the need

for repeat revascularization was greater among OPCAB patients (93.6%) than CABG patients (89.9%).³³⁸ Several large retrospective reviews of traditional CABG versus OPCAB procedures have found a gender-specific survival benefit for women who undergo OPCAB surgery, compared with those who undergo on-pump CABG.³³⁹⁻³⁴¹

A recent 5-year trial of more than 4000 patients from 19 different countries found no difference in stroke, MI, renal failure, repeat revascularization, and death at 5 years of follow up of patients who underwent on-pump versus off-pump CABG.³⁴²

Minimally Invasive Coronary Artery Bypass Surgery.

The most popular alternative approach to sternotomy is the minimally invasive coronary artery bypass (MIDCAB) through a left anterior thoracotomy, which allows direct-access IMA harvesting and grafting to the LAD artery. Some surgeons harvest the left IMA (LIMA) by using robot-assisted endoscopic technology before making the small incision to complete the LIMA-to-LAD anastomosis through the left anterior thoracotomy incision. In these cases, deflation of the left lung is required for visualization of the anastomosis, accomplished with a double-lumen endotracheal tube or a bronchial blocker. In addition, carbon dioxide is insufflated into the left hemithorax during the period while the lung is deflated.

Usually, the MIDCAB technique involves grafting of only a single vessel, and exposure for this anastomosis may be suboptimal.³³² Challenges for the anesthesiologist in MIDCAB cases include the need for single-lung ventilation while the LIMA is dissected, and the anastomosis is performed. Because the graft is only to the LAD in these cases, no extreme positioning of the heart occurs that could significantly compromise hemodynamic status. However, external defibrillator or pacing pads should be attached to the patient before preparing and draping because surgical access to the heart is limited during these procedures.³⁴³

Since the MIDCAB procedures were first introduced, as the technology has evolved so have the surgical techniques and the anesthetic techniques. Still, there are a variety of different ways to manage anesthetics for MIDCAB operations and different institutions have different techniques that they employ to take care of these patients.

In addition to standard ASA monitors, these patients are monitored with an arterial line (preferably in the radial artery), a central line introducer, and potentially a PA catheter.

Patients presenting for MIDCABs are induced in a routine fashion, as for any patient undergoing CABG surgery. In order to maximize surgical exposure by lung isolation, cardiac anesthesiologists prefer to intubate with double lumen endotracheal tubes or use bronchial blockers for MIDCAB surgeries.³⁴⁴ Maintenance of anesthesia must keep in mind that the MIDCAB is an off-pump case. Hemodynamic control is achieved by fluid administration and pharmacology. Norepinephrine and phenylephrine have both been used effectively for these cases. Procedures for extubation after MIDCAB vary from institution to institution.

OUTCOMES OF MIDCAB. Multiple studies over the years have evaluated the outcomes of MIDCAB, both in the United

States and abroad. MIDCAB has shown promise when compared to the conventional CABG surgery. MIDCAB is associated with less morbidity and mortality when compared to on-pump and off-pump CABG procedures.^{345,346}

TOTAL ENDOSCOPIC CORONARY ARTERY BYPASS. Total endoscopic coronary artery bypass (TECAB) is currently the most minimally invasive approach to performing CABG. TECAB is performed via a few port sites (Fig. 54.24),³⁴⁷ with the surgeon remotely controlling the ports via a robotic system.³⁴⁷

TECAB is performed in three different ways: arrested heart TECAB, beating heart TECAB with CPB, and beating heart TECAB without CPB. Defibrillation pads are placed on the patient in the preoperative period. In cases where the heart is arrested, a remotely accessed perfusion technique is used with the help of an endoaortic occlusion balloon clamp (EAOCB) (Fig. 54.25).³⁴⁷

The EAOCB is placed via the femoral vessels, or via the axillary artery if accessing the femoral vessels or the descending aorta is contraindicated or not possible. TEE can provide useful information to guide placement of the EAOCB.



Fig. 54.24 TECAB is performed via a few port sites, with the surgeon remotely controlling the ports via a robotic system.

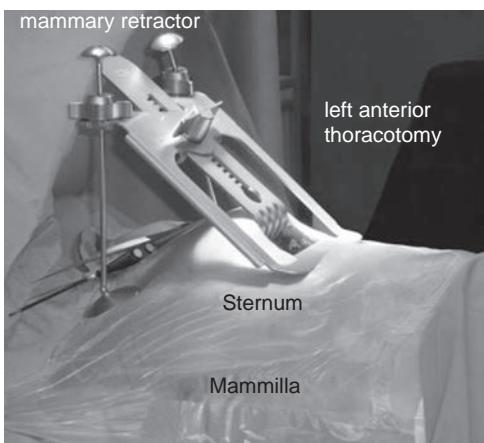


Fig. 54.25 Remotely accessed perfusion technique with an endoaortic occlusion balloon clamp (EAOCB).

ANESTHETIC CONSIDERATIONS. Anesthetic management of patients undergoing TECAB differs from general anesthesia for routine cardiac cases. General anesthesia is induced in routine fashion. Since one lung ventilation is needed for these procedures, this goal is achieved by either using a double lumen endotracheal tube, or a bronchial blocker, similar to the MIDCAB. At least one large-bore peripheral intravenous line, a central line with an introducer, and bilateral radial arterial lines are required for TECAB procedures. Bilateral radial arterial lines are used to monitor the position of the EAOCB to ensure that it doesn't migrate and occlude the innominate artery. TECAB cases may require placement of a PA vent or a coronary sinus catheter. Supplemental regional anesthesia has been reported to have been successfully employed in TECAB cases, which can facilitate early extubation in these patients.³⁴⁷ Extubation of TECAB patients is mostly dictated by patients' comorbidities.

TEE IN TECAB. TEE serves as a crucial tool in the management of patients undergoing minimally invasive procedures. In addition to the usual monitoring and diagnostic capabilities of TEE, it is also used to monitor major vascular structures and to guide cannulas and catheters during the cannulation process.

In cases where the EAOCB is used, TEE provides real-time imaging of the position of the balloon, which serves as a critical monitor for migration or malposition.

OUTCOMES OF TECAB. Similar to MIDCAB there is a paucity of large-scale randomized studies looking at the outcome data for TECAB procedures. Studies looking at smaller number of patients are promising, though acknowledge their limitations.³⁴⁸

Hybrid Coronary Revascularization. Hybrid coronary revascularization combines MIDCAB techniques with catheter-based interventions.³⁴⁹ Ideally, a hybrid operating room is used. The surgical component of the hybrid procedure may be offered in a completely endoscopic fashion, using robotic technology. The goal of such procedures is a very short recovery time.³⁴⁹ Although the perioperative results and intermediate-term outcomes of hybrid procedures appear to meet the standards of CABG performed with CPB, no data on long-term outcomes are available.

Patients undergoing OPCAB, MIDCAB, or hybrid coronary revascularization do not undergo CPB, and thus may suffer from temperature alterations that cannot be treated using the CPB perfuse temperature. Therefore, heating blankets for patients and a warm operating room environment are essential to prevent unacceptable reductions in body temperature.

ANESTHETIC MANAGEMENT OF HYBRID CORONARY REVASCULARIZATION. As mentioned earlier, HCAR combines coronary revascularization via a minimally invasive surgical approach and catheter-based coronary intervention. HCAR can be done in a staged manner.

A two-stage model used commonly in the early days of the procedure requires the patient to have either surgery or PCI and then return at a later date for the other part of the procedure. This entails two separate admissions, two separate procedures, along with the concomitant patient and family inconvenience. Anesthesiologists are involved in the surgical procedures in a hybrid revascularization, though they are rarely involved in the PCI. The one-stage

model allows for both the surgical and the PCI revascularization to be done in one admission, typically in one sitting in a hybrid operating room. Patients can be exposed to one anesthetic and can undergo the surgical procedure and the PCI sequentially, in either order.

HYBRID CORONARY REVASCULARIZATION OUTCOMES. Though large-scale studies are lacking at this time, smaller institutional-based studies looking at outcomes are increasing, thus adding to the body of literature in this regard. A review of the available data suggests that HCAR outcomes are promising, which is not surprising since HCAR takes advantage of the benefits of CABG and PCI while minimizing the risks of each. If outcomes are similar or superior to those of conventional revascularization, then a careful cost-benefit analysis will take place to determine the role that HCAR holds in our armamentarium.³⁵⁰

CARDIAC VALVE LESIONS

Mitral Valve Disease

In the United States and other industrialized nations, mitral valve disease is usually caused by primary degenerative (i.e., age-associated) or inherited mitral valvular abnormalities or, increasingly, by ischemic heart disease resulting in functional mitral incompetence. In developing countries, conversely, rheumatic heart disease is relatively more prevalent and therefore a more common cause of mitral valve disease.³⁵¹ Primary or “organic” mitral valve disease involves abnormalities in the valve itself or in its subvalvular structural components.³⁵² Mitral valve prolapse, myxomatous degeneration of the mitral valve, rheumatic mitral insufficiency, cleft mitral valve associated with an AV septal defect, and any infiltrative or fibrotic processes caused by systemic diseases are all associated with inherent structural abnormalities of the mitral valve.

Anatomy of the Mitral Valve

Mitral valve anatomy includes the leaflets, commissures, chordae, annulus, papillary muscles, and the LV. The mitral valve has two leaflets, the anterior mitral leaflet (AML) and the posterior mitral leaflet (PML). Both leaflets are subdivided according to the Carpentier classification. The PML is divided into three scallops: the anterior or medial scallop (P1), the middle scallop (P2), and the posterior or lateral scallop (P3). The corresponding AML sections that oppose these PML scallops are similarly called A1, A2, and A3 (Figs. 54.26 and 54.27). The AML is broad in shape, occupies a larger portion of the mitral valve area (MVA) than the PML, yet attaches itself to only two-fifths of the annulus. The PML, though smaller in area, is crescentic in shape and attaches to three-fifths of the annulus. Fig. 54.28³⁵³ shows the components of the mitral valve leaflets using three-dimensional echocardiography. Common nomenclature is used to ensure accurate communication between the surgeon and the echocardiographer.

The commissures of the mitral valve define the area where the leaflets come together at their annular insertion sites. Chordae tendineae originate from the papillary muscle heads and attach to the mitral leaflets. Chordae are generally divided into three types. Primary chordae attach to the free margins of the leaflets, thus preventing the prolapse of the margins and ensuring alignment of the “rough edges”

for coaptation. Secondary chordae attach to the body or the ventricular surfaces of the two leaflets and prevent billowing during systole, additionally providing a reduction in tension. Tertiary or basal chordae extend from the papillary muscle to the annulus of the valve.

The mitral annulus is the anatomical junction between the LA and the LV and attaches to the mitral valve leaflets in an anterior and a posterior segment. The anterior segment also provides the attachment to the fibrous trigones. There are two fibrous trigones, the right and the left. Parts of the mitral, tricuspid, aortic annuli, and the membranous portion of the interventricular septum comprise the right fibrous trigone. The fibrous left border of the aortic-mitral curtain makes up the left fibrous trigone. The fibrous skeleton of the heart is not continuous in the region of the posterior mitral annulus, thus this area is relatively weaker and prone to enlarge with the dilatation of the left heart. The overall shape of the mitral annulus is saddle-like, and during systole, the mitral annulus contracts as the commissures move toward the apex.

The anterolateral and the posteromedial papillary muscles attach to the LV free wall between the middle third and the apex of the ventricle. The anterolateral papillary muscle has one body (or head) while the posteromedial muscle can have two or more bodies. Blood supply to the anterolateral muscle can originate from one or more branches of the left coronary artery, while the posteromedial papillary muscle only has a single blood supply (i.e., from the circumflex coronary artery). This explains the vulnerability of the posteromedial papillary muscle to ischemia and infarction. Due to the intricate connections of the papillary muscles to the LV, changes in ventricular geometry can cause distortion and abnormal functioning of the mitral valve.³⁵⁴

Mitral Stenosis

PATHOPHYSIOLOGY. The disease process of rheumatic mitral stenosis (MS) includes thickening, commissural fusion, and increased rigidity of the mitral valve leaflets, as well as thickening, fusion, and contracture of the

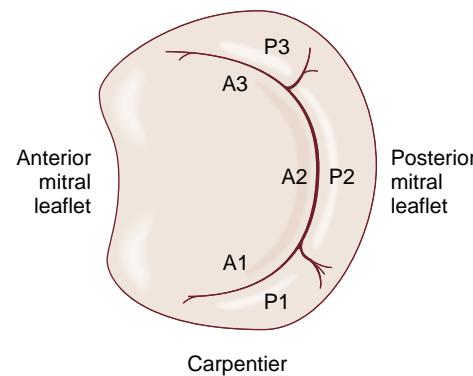


Fig. 54.26 Standard terminology as applied to the mitral valve leaflets is illustrated in this image. The anterior and posterior mitral valve leaflets are each divided into three segmental regions. (From Savage RM, Aronson S, Thomas JD, et al, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. Baltimore: Lippincott Williams & Wilkins; 2005.)

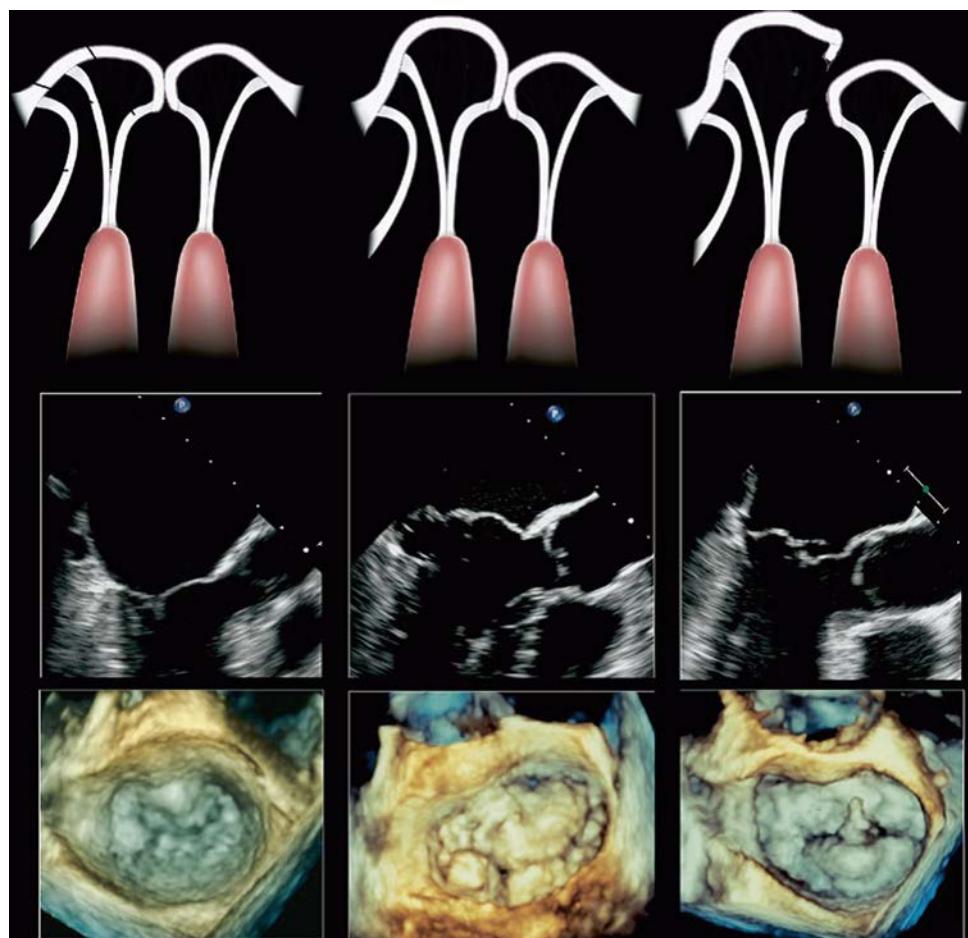


Fig. 54.27 Intra-operative 2D and 3D TEE depiction of MV prolapse and leaflet flail. (From O'Gara P, Sugeng L, Lang R, et al. The role of imaging in chronic degenerative mitral regurgitation. *JACC Cardiovasc Imaging*. 2008;1[2]:221–237.)

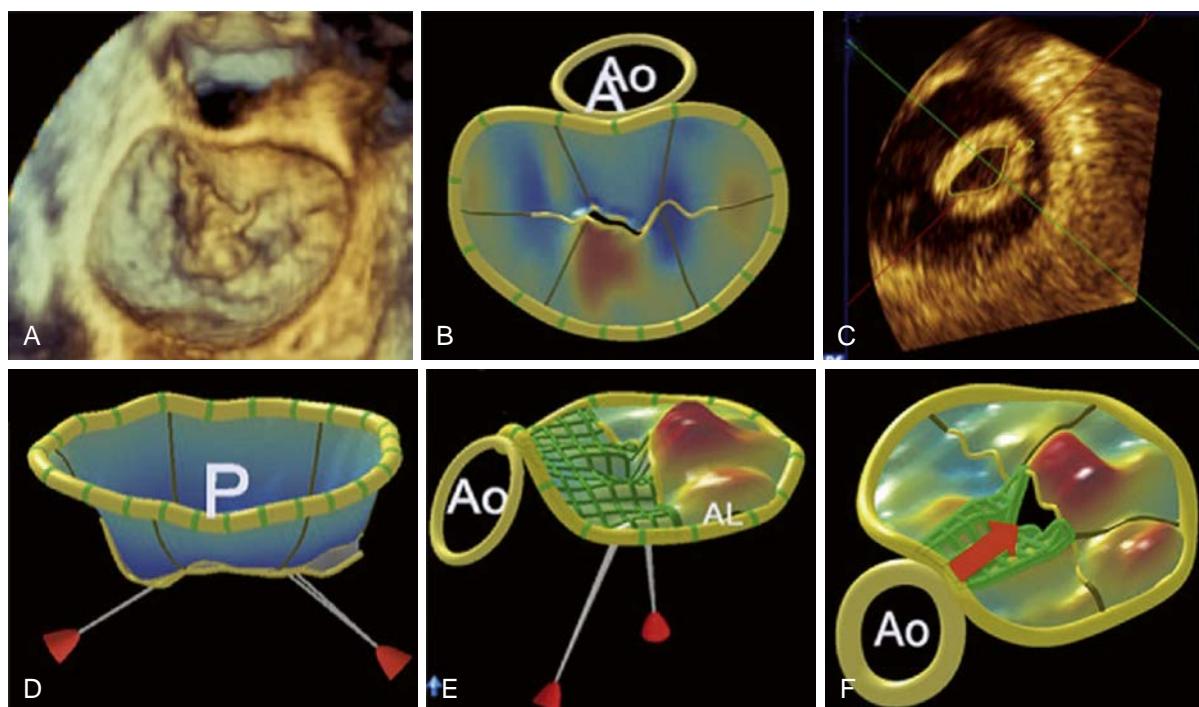


Fig. 54.28 The components of the mitral valve leaflets using three-dimensional echocardiography. *A*, Atrial aspect of the Mitral valve. Prolapsing P2 scallop can be seen. *B*, 3D reconstruction of the Mitral valve showing P2 scallop in red. *C*, Ventricular aspect of the Mitral valve. *D*, Side view of the 3D reconstruction of the Mitral valve with the chordae in view. *E*, View from the anterolateral commissure of the Mitral valve, with prolapsing scallop in red. *F*, Atrial view of the valve showing prolapsing scallops and the failure of coaptation of leaflets causing the regurgitant jet.

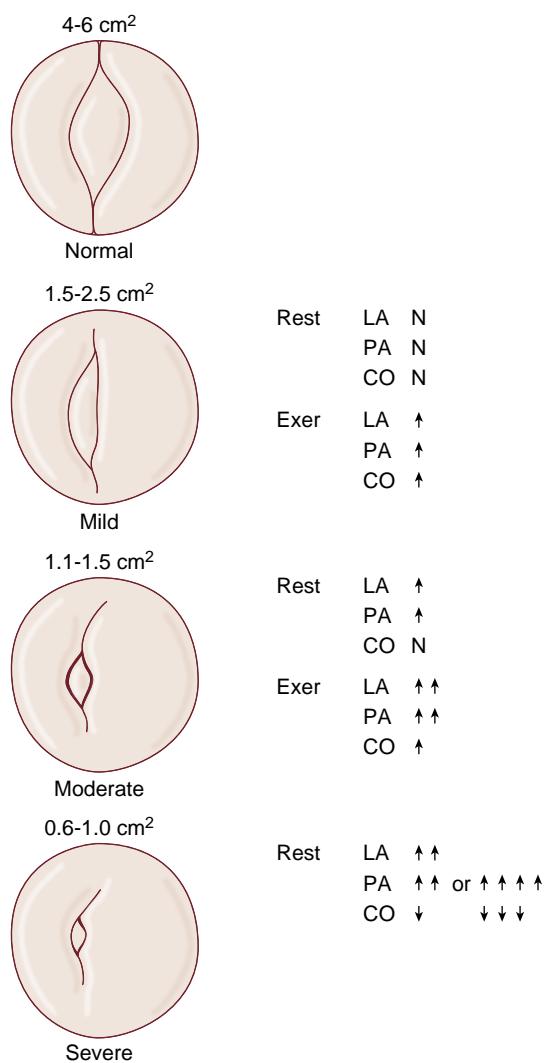


Fig. 54.29 Diagrammatic representation of the hemodynamic changes that occur at various stages of severity of mitral stenosis. The valve area is listed above each stage. ↑, Increased; ↓, decreased; CO, cardiac output; Exer, exercise; LA, left atrial pressure; N, normal; PA, pulmonary arterial pressure. (From Rappaport E. Natural history of aortic and mitral valve disease. *Am J Cardiol*. 1975;35:221–227.)

chordae and papillary heads. Furthermore, with long-standing rheumatic disease, some degree of calcification of the valve apparatus inevitably occurs. Physiologically, these changes result in obstruction at the level of the mitral valve.

The normal mitral valve orifice area is approximately 4 to 5 cm².³⁵⁵ Symptoms can occur if the valve area is less than 2.5 cm² and can be precipitated by clinical events associated with increased CO and consequent increased flow across the valve; these events include stress, exercise, anemia, pregnancy, and febrile illness (Fig. 54.29). Symptoms do not usually occur at rest unless the MVA is less than 1.5 cm². Obstructed flow across the mitral valve is associated with a pressure differential or gradient across the valve. The more severe the MS, the greater the gradient, as long as flow across the valve is held constant. Grading of MS is shown in Table 54.14.³⁵³

Transmitral pressure gradients through the mitral valve depend on the volume flow rate. Severe MS may be present

with a low measured or calculated gradient across the valve, as in patients with right HF and pulmonary hypertension. An MVA estimate is a more independent measure of the severity of MS. Currently, MS is primarily diagnosed and monitored with echocardiography, although MVA can be calculated during catheterization by using the Gorlin equation.³⁵⁶ Assessing MS severity by echocardiography involves two-dimensional planimetry of the valve orifice and Doppler-derived measurements of gradient, pressure half-time, and deceleration time. The advent of three-dimensional technology has enabled clinicians to visualize the mitral valve anatomy more accurately (Fig. 54.30).³⁵⁴

Management considerations in MS emphasize the pathophysiological changes that occur in the left atrium, the pulmonary vasculature, the right heart, and the LV. Obstructed mitral inflow with secondary increases in LA pressure (LAP) gradually causes enlargement of the left atrium, which can lead to the onset of atrial fibrillation, thromboembolic complications, or both if low blood flow velocity causes clot formation in the atrium or appendage.

Patients with MS and chronic atrial fibrillation are at increased risk of embolic stroke, at a rate of 7% to 15% per year.³⁵⁶ Treatment may include anticoagulation with intravenous heparin or oral warfarin, pharmacologic rate control, and pharmacologic or electrical cardioversion for hemodynamically significant or acute-onset atrial fibrillation. In patients scheduled for cardioversion, TEE may need to be performed first to rule out the presence of LA thrombus.³⁵⁵

Elevated LAP leads to passive increases in pulmonary venous and arterial pressures. Most patients with MS have a greater PAP than would be expected if PAP were estimated solely from elevations in LAP. These exaggerated pressures are secondary to reactive pulmonary vasoconstriction or histologic changes in the medial and intimal layers of pulmonary arteries and arterioles. PAP sometimes correlates with the severity of MS, but pressures can range widely because of factors such as transmural pressure gradient, LVEDP, the actual MVA, and a history of chronic pulmonary disease.

The chronic elevation in PAP caused by MS leads to compensatory and decompensatory changes in the right ventricle. Exposure to elevated pressure leads to compensatory RV hypertrophy; however, the response in the right ventricle is less efficient than in the LV because of the shape, wall thickness, and smaller muscle mass of the right ventricle. Because of the right ventricle's relative vulnerability, chronic pulmonary hypertension invariably leads to progressive RV dilation and eventual RV failure.

The effect of MS on the LV is primarily the result of obstruction of diastolic inflow. The narrowed mitral valve orifice leads to prolonged early diastolic mitral inflow and delayed filling of the LV. Late diastolic filling, which occurs during atrial systole, is obviously compromised in patients who have atrial fibrillation secondary to MS. In cases of MS, pressure-volume loops are shifted to the left, so LVEDP and LV end-diastolic volume (LVEDV) are lower. Stroke volume is diminished, especially in clinical situations that result in elevated heart rate and shortened diastolic filling intervals (Fig. 54.31).³⁵⁷

LV function or contractility is assumed to be normal in most patients with MS. However, in a review of the literature,

TABLE 54.14 Grading of Mitral Stenosis

Severity	MVA, cm ²	Gradient, mm Hg	PAP	Symptoms	Signs	Therapy
Mild	>1.8	2-4	Normal	Usually absent	S ₂ -OS >120 ms; normal P ₂	IE prophylaxis
Moderate	1.2-1.6	4-9	Normal	Class II	S ₂ -OS 100-120 ms; normal P ₂	IE prophylaxis; diuretics
Moderate to severe	1.0-1.2	10-15	Mild pulmonary HTN	Class II-III	S ₂ -OS 80-100 ms; P ₂ increase	IE prophylaxis; BMV if applicable or surgery if more than mild Sx
Severe	<1.0	>15	Mild to severe pulmonary HTN	Class II-IV	S ₂ -OS <80 ms; P ₂ increase; RV lift Sx if R heart fails	IE prophylaxis; BMV or surgery

HTN, Hypertension; IE, infective endocarditis; MVA, mitral valve area; OS, opening snap; PAP, pulmonary artery pressure; RV, right ventricular; Sx, symptoms. From Carabello BA. Modern management of mitral stenosis. *Circulation*. 2005;112:432-437.



Fig. 54.30 Three-dimensional image of a stenotic mitral valve from the left atrial perspective. (From Lang RM, Tsang W, Weinert L, et al. Valvular heart disease: the value of 3-dimensional echocardiography. *J Am Coll Cardiol*. 2011;58:1933-1944.)

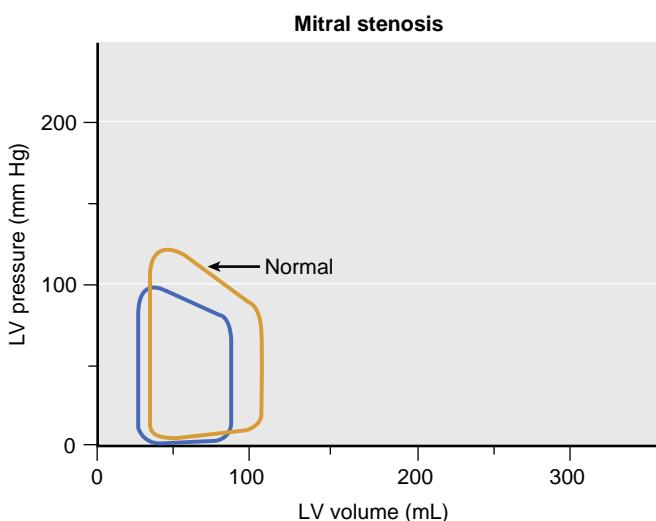


Fig. 54.31 Pressure-volume loop in mitral stenosis. LV, Left ventricular. (From Jackson JM, Thomas SJ, Lowenstein E. Anesthetic management of patients with valvular heart disease. *Semin Anesth*. 1982;1:239.)

Klein and Carroll showed that the assumption of preserved LV contractility in patients with MS is debatable.³⁵⁸ Instead, the prevalence of LV dysfunction in patients with MS may be as high as 30%. Proposed mechanisms include reduced filling of the LV, muscle atrophy, inflammatory myocardial fibrosis leading to wall-motion abnormalities, scarring of the subvalvular apparatus, abnormal patterns of LV contraction, reduced LV compliance with diastolic dysfunction, increased LV afterload leading to ventricular remodeling, right-to-left septal shift secondary to the effect of pulmonary hypertension on the right ventricle, and coexistent diseases such as systemic hypertension and CAD.³⁵⁸ The hemodynamic changes associated with MS are summarized in Fig. 54.29.

ANESTHETIC MANAGEMENT. An understanding and appreciation of the pathophysiologic changes associated with MS form the foundation of anesthetic management in these patients (Table 54.15). Primary concerns in patients with MS include managing ventricular preload, heart rate, and coexisting pulmonary hypertension, as well as potentially diminished RV and LV contractile function. Most patients with valvular heart disease have increased dependency on and sensitivity to ventricular preload. Flow through a stenotic mitral valve requires a higher-than-normal pressure gradient between the left atrium and the LV. Thus, reduction in preload, either from blood loss or from the venodilatory effects of anesthesia, can markedly affect stroke volume, CO, and tissue perfusion. However, in higher grades of MS, LAP may be very high, and the difference between adequate filling pressure and an LAP that leads to congestive failure may be small. Thus, judicious fluid management is required.

In patients with MS, the heart rate should be kept within its normal range. Tachycardia may be poorly tolerated because of the decreased time for diastolic filling. Moreover, pressure gradients are somewhat flow dependent in MS. Elevated flow states, such as pregnancy and increased sympathetic activity from any source, can dramatically increase the pressure gradient across the valve and are reflected in elevated LAP or pulmonary venous pressure. From data obtained by continuous wave Doppler interrogation of the inflow velocities across the mitral valve, the pressure gradient is derived through the use of a modified form of Bernoulli's equation, $\Delta P = 4v^2$, where v is the measured velocity of blood flow through the valve. Thus, any increase in transvalvular flow rate caused by an increase in heart

TABLE 54.15 Pathophysiologic Changes Associated With Mitral Stenosis

	LV Preload	Heart Rate	Contractility	Systemic Vascular Resistance	Pulmonary Vascular Resistance
Mitral stenosis	↑	↓	Maintain	Maintain	↓

LV, Left ventricular.

From Townsley MM, Martin DE. Anesthetic management for the surgical treatment of valvular heart disease. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:340.

rate has a significant impact on transvalvular flow dynamics and on LAP.

Atrial contributions to stroke volume may be elevated in patients with MS who are in the early stages of the disease and are not in atrial fibrillation. When atrial fibrillation has occurred, the atrial kick is lost. However, the most important factor in the deterioration of the patient's clinical condition is tachycardia itself, rather than loss of the atrial kick.

Contractility and SVR are usually preserved in MS. If anything, the LV is chronically underloaded, but wall motion abnormalities or global systolic dysfunction develop in a small percentage of MS patients. Usually, SVR is not a factor in augmenting forward flow because stroke volume is determined by the mitral valve orifice area and the diastolic filling interval. It may be appropriate to lower SVR for an LV that has marked systolic dysfunction, but care must be exercised because a reduction in afterload is inevitably accompanied by a reduction in preload, which may not be desirable in patients with significant MS.

RV dysfunction probably poses a greater challenge in treating patients with MS than does LV dysfunction. The chronic elevations in LAP can be persistent in patients with long-standing pulmonary hypertension. In the patient with residual pulmonary vascular disease and irreversible pulmonary hypertension, supporting a failing or marginally functional right ventricle becomes the top clinical priority.

Monitoring includes standard noninvasive modalities and invasive monitoring of blood pressure, CVP, and intraoperative echocardiography. Monitoring PAP and using a PA catheter to monitor CO may be very helpful, but care and judgment must be exercised, given the propensity for PA rupture in patients with long-standing pulmonary hypertension. Inotropic support may be needed for patients with secondary RV dysfunction or failure. Epinephrine and milrinone are good therapeutic options. Management of RV dysfunction includes optimizing acid-base balance and using hypocapnia, hyperoxia, and possibly vasodilators to decrease PVR.

Mitral Regurgitation. The complex anatomic structure of the mitral valve is especially pertinent in any consideration of the pathophysiology and management of patients who present for operative intervention for MR. The mitral apparatus consists of six primary components: the LA wall, the annulus of the mitral valve, the mitral valve leaflets, the chordae tendineae, the papillary muscles, and the wall of the LV. Abnormalities or dysfunction in any component can result in mitral valve incompetence.

MR can be classified as either organic (intrinsic valvular disease) or functional (i.e., related to nonvalvular components of the mitral apparatus).³⁵⁹ It is common for MR to have a functional and an organic component, as in

TABLE 54.16 Acute and Chronic Mitral Regurgitation

Characteristic	Chronic Compensated	Chronic Decompensated	Acute
Symptom onset	None	Gradual DOE	Abrupt CHF
PHYSICAL EXAMINATION			
Blood pressure	Normal	Normal	↓
Pulmonary congestion	None	Variable	↑↑↑↑
HEMODYNAMICS			
LA pressure	Normal	↑	↑↑
v wave	Absent	Variable	↑
ECHOCARDIOGRAPHY			
LV size	↑	↑↑	Normal
LA size	↑	↑	Normal
MR jet v wave	Absent	Variable	↑

CHF, Congestive heart failure; DOE, dyspnea on exertion; LA, left atrial; LV, left ventricular; MR, mitral regurgitation; arrows indicate relative increase (↑) or decrease (↓) in comparison with normal.

From Otto CM. Valvular heart disease: prevalence and clinical outcomes. In: Otto CM, ed. *Valvular Heart Disease*. 2nd ed. Philadelphia: Saunders; 2004:1–17.

rheumatic valve disease resulting in annular or LV dilation with superimposed abnormalities of leaflet coaptation. In developed countries, the most common causes of MR are as follows: (1) myxomatous degeneration of the mitral valve resulting in annular dilation, chordal elongation and rupture, and redundant, prolapsing, or flail mitral valve leaflets; and (2) mitral insufficiency caused by ischemic heart disease. The most common indication for surgical repair or replacement of the regurgitant mitral valve is myxomatous degeneration, which includes mitral valve prolapse syndromes.³⁶⁰ Chronic ischemic or functional MR is present in 10% to 20% of patients with CAD and, unlike MR with primary valvular causes, it does not involve abnormalities in the morphology of the mitral valve.³⁶¹ Nonetheless, the long-term morbidity and mortality associated with this type of MR are significant.³⁵²

The severity of MR is assessed in the context of whether the MR is acute or chronic. Symptom presentation, physical examination, hemodynamics, and echocardiography all provide useful information for ascribing a severity grade (Table 54.16). Echocardiographic assessment is particularly important for guiding intraoperative decisions about the need for intervention and the adequacy of repair or replacement of the mitral valve (Fig. 54.32). As with MS, several echocardiographic parameters, both two-dimensional and Doppler-derived, can be used to grade the severity of MR (Table 54.17). The advent of three-dimensional technology

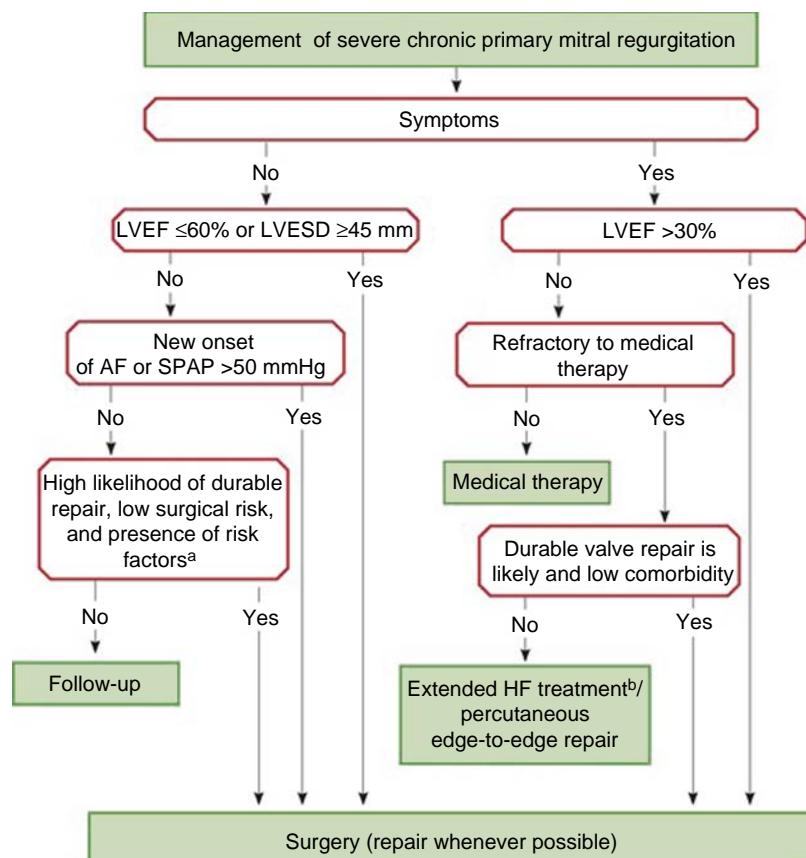


Fig. 54.32 Management of severe chronic primary mitral regurgitation. ^aWhen there is a high likelihood of durable valve repair at a low risk, valve repair should be considered (IIa C) in patients with LVESD ≥ 40 mm and one of the following is present: flail leaflet or LA volume ≥ 60 mL/m² BSA at sinus rhythm. ^bExtended HF management includes the following: CRT; ventricular assist devices; cardiac restraint devices; heart transplantation. AF, Atrial fibrillation; BSA, body surface area; CRT, cardiac resynchronization therapy; HF, heart failure; LA, left atrial; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; SPAP, systolic pulmonary arterial pressure. (Redrawn from Baumgartner H, Falk H, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739–2791.)

TABLE 54.17 Classification of the Severity of Mitral Valve Regurgitation in Adults

MITRAL VALVE REGURGITATION			
	Mild	Moderate	Severe
QUALITATIVE			
Angiographic grade	1+	2+	3-4+
Color Doppler jet area	Small central jet (<4 cm ² or <20% left atrial size)	Signs of MR greater than mild but no severe MR	Vena contracta width >0.7 cm with large central jet (area >40% of left atrium) or with a wall-impinging jet swirling in left atrium
Doppler vena contracta width (cm)	<0.3	0.3-0.69	≥0.7
QUANTITATIVE			
Regurgitant volume (mL/beat)	<30	30-59	≥60
Regurgitant fraction (%)	<30	30-49	≥50
Regurgitant orifice area (cm ²)	<0.2	0.2-0.39	≥0.4
ADDITIONAL CRITERIA			
Left atrial size		Enlarged	
Left ventricular size		Enlarged	

MR, Mitral regurgitation.

From Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;52:e1-142.

and current calculation software greatly improved clinicians' ability to assess the severity and identify the precise cause of MR (Fig. 54.33; see also Fig. 54.32).

PATHOPHYSIOLOGY. The incompetent mitral valve allows retrograde passage of blood from the LV into the left atrium during systole. The magnitude of the regurgitant volume is a function of the size of the regurgitant orifice, the pressure differential between the left atrium and the LV, and the duration of the regurgitant cycle.³⁵⁹ Thus, higher systolic driving pressures, as in hypertension, can increase the regurgitant volume. Loading conditions are important as well, especially whenever functional changes in annular and LV geometry are important components of the mechanism of MR. These conditions should be considered during the intraoperative evaluation of MR because anesthetic effects on afterload and preload can drastically alter the severity of MR from its baseline level, as seen in preoperative echocardiographic or catheterization assessments. (Table 54.18)

LV function and pressure tend to be normal in patients with chronic MR. EF is often normal or supranormal unless the ventricle has decompensated with chronic MR or is acutely ischemic. A normal EF can be misleading, and masked ventricular dysfunction may be revealed after valve repair or replacement. The left atrium serves as a low-pressure pathway during systolic ejection, so that EF overestimates ventricular function.

When MR has an acute onset, LAP is elevated, because LA compensatory changes have had no time to occur. A v-wave may be present on the LAP, PAP, or PCWP recordings. In contrast, in chronic MR, the LAP increases are less dramatic because of compliance changes in the left atrium as a function of chamber dilation.

The long-term sequelae of MR are related to chronic pressure and volume effects on the left atrium and the LV. The LV is exposed to a chronic, isolated volume-overload state. Eccentric hypertrophy of the LV develops, causing chamber enlargement without significant increases

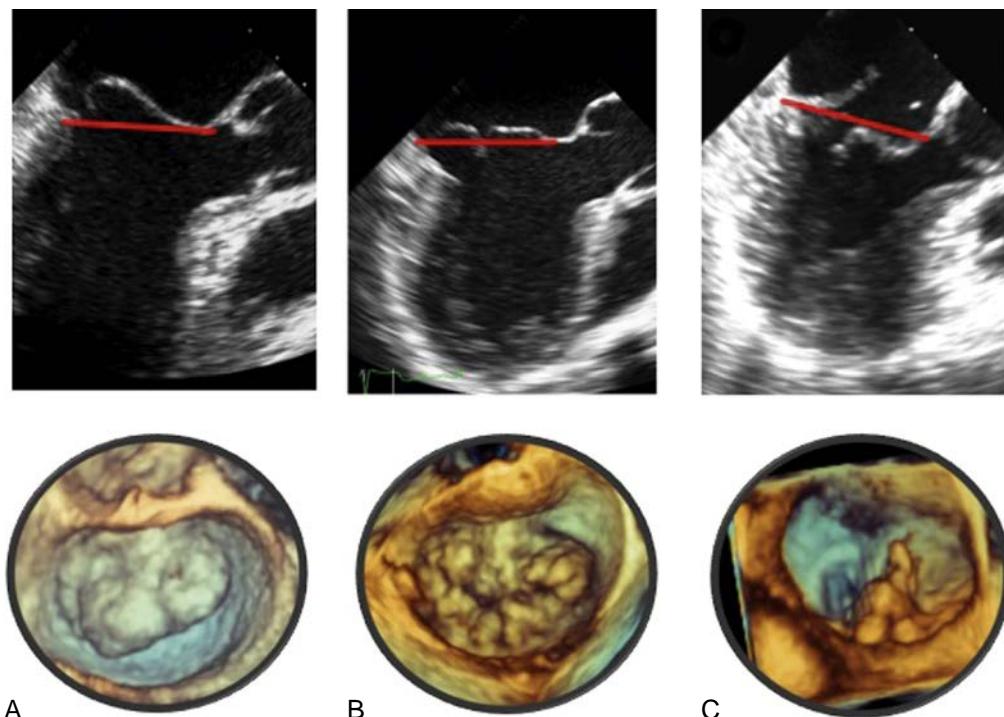


Fig. 54.33 Differential diagnosis of mitral leaflet prolapse. Two-dimensional (2D) transesophageal echocardiography (TEE) long-axis view demonstrating anterior leaflet prolapse (A, top) with a three-dimensional (3D) transesophageal example as seen from the left atrium (A, bottom). Leaflet prolapse should be diagnosed when the free edge of the leaflet overrides the plane of the mitral annulus during systole. 2D TEE long-axis view demonstrating bileaflet billowing of the mitral valve with prolapse resulting from chordae tendineae elongation (B, top) with a 3D transesophageal example as seen from the left atrium (B, bottom). Leaflet billowing is diagnosed when systolic excursion of the leaflet body occurs into the left atrium resulting from excess leaflet tissue, with the leaflet free edge remaining below the plane of the mitral annulus. 2D TEE long-axis view demonstrating flail valve resulting from chordae rupture (C, top) with a 3D transesophageal example of P2 flail as viewed from the left atrium (C, bottom). (From Lang RM, Tsang W, Weinert L, et al. Valvular heart disease: the value of 3-dimensional echocardiography. *J Am Coll Cardiol*. 2011;58:1933–1944.)

TABLE 54.18 Pathophysiologic Changes Associated With Mitral Regurgitation

LV Preload	Heart Rate	Contractility	Systemic Vascular Resistance	Pulmonary Vascular Resistance
Mitral regurgitation	↑ or ↓	↑, maintain	Maintain	↓

LV, Left ventricular.

From Townsley MM, Martin DE. Anesthetic management for the surgical treatment of valvular heart disease. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:346.

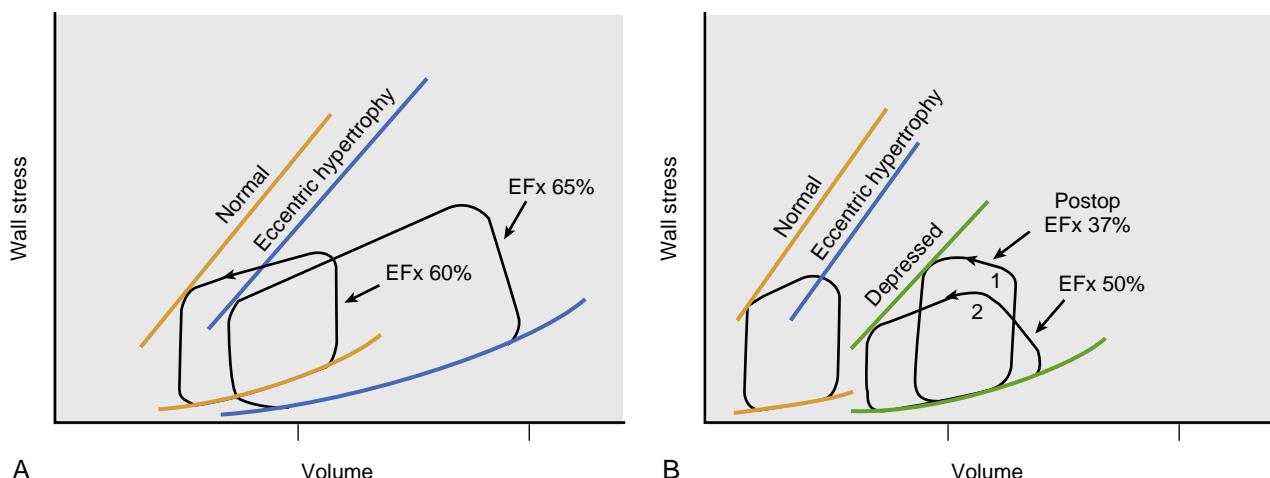


Fig. 54.34 Diagram of wall stress–volume loops and end-systolic volume–wall stress relationships in severe mitral regurgitation. (A) As in aortic regurgitation, the shift to the right of the diastolic and end-systolic relationships allows the volume-overloaded left ventricle to maintain a high stroke volume. Mean wall stress during ejection is somewhat reduced, and in mitral regurgitation the ejection fraction (EFx) is high normal when contractility is normal. (B) With the development of depressed contractility, the end-systolic wall stress–volume relationship is shifted to the right preoperatively. Despite severely depressed contractility, the ventricle is able to deliver a nearly normal EFx because of the very large ventricular volume and the relatively low mean wall stress during ejection (beat 2, EFx = 50%). Contractility remains depressed after mitral valve replacement (Postop), and with correction of the low-impedance leak, the ventricle must now deliver the total stroke volume into the aorta against higher wall stress; the EFx therefore falls to 37% (beat 1).

in wall thickness. Forward CO is preserved because of eccentric hypertrophy and the low impedance of the left atrium—a physiologic equivalent of afterload reduction. The larger stroke volume ejected by the LV is composed of the normal venous return into the left atrium in addition to the regurgitant volume from the previous cardiac cycle. In the early stages of MR, LVEDP is relatively normal because of compliance changes of the LV. With time, however, compensatory eccentric hypertrophy fails to preserve LV systolic function, and gradual systolic failure ensues, as noted on pressure-volume loops (Fig. 54.34). In patients with MR, deciding on the timing of surgical intervention is an important duty of the referring cardiologist because LV systolic performance can deteriorate to a point that full functional recovery after valve surgery may not be possible.

The LA is exposed to increases in volume and pressure. The LA dilates to compensate for the regurgitant volume during systole, and in the early stages of MR, preservation of near-normal LAP and protection of the pulmonary vasculature is likely. Progressive LA enlargement commonly leads to atrial fibrillation, which occurs in approximately 50% of patients who are about to undergo surgical correction of MR. However, patients with MR appear to be at a lower risk for thromboembolic complications than are patients with MS.

When LAP compliance thresholds are reached, LAP and PAP become elevated. Eventually, if chronically exposed to elevated PAP, the right ventricle progressively enlarges, and RV dysfunction develops.

Carpentier classifies MR into three different types by the mechanism causing regurgitation. Type I MR is characterized by “normal leaflet motion” and annular dilatation as the cause of regurgitation. Type II MR is caused by excessive motion of the margin of a leaflet and is the most common of the three etiologies. In the type II etiology excessive motion causes the leaflet to rise above the annular plane. Type III

MR is characterized by restricted motion of the mitral leaflet. It is further subdivided into two components: Type IIIa is due to fibrosis of the subvalvular apparatus of the mitral valve, whereas IIIb is due to tethering of the leaflet to the ventricular wall as a result of remodeling of the ventricle (ischemic etiology).³⁵⁴

Fig. 54.27³⁵⁴ shows the above mentioned Carpentier classification.

ANESTHETIC MANAGEMENT. In the anesthetic management of MR, the primary goal is maintaining forward systemic flow. In chronic, compensated MR, maintaining preload, judiciously reducing afterload, and keeping the heart rate in the high-normal range may be adequate (see Table 54.18).

As with most compensated forms of valvular heart disease, patients with hemodynamically significant MR are sensitive to ventricular loading conditions. Augmenting preload may be prudent in the interval before anesthetic induction. However, MR is dynamic; ventricular distention can lead to the expansion of an already dilated mitral annulus and thus worsen MR.

The heart rate should be maintained in the high-normal range (i.e., 80–100 beats/min). Bradycardia has dual detrimental effects on MR: it lengthens the systolic period, thus prolonging regurgitation, and it increases the diastolic filling interval, which can lead to LV distention. A sinus rhythm is preferred, but with less dependency on the atrial kick in chronic, compensated MR than in stenotic valvular heart disease.

LV contractility may be preserved in early compensated MR. However, EF indices are poorly correlated with LV systolic function in patients with moderate to severe MR, and underlying systolic dysfunction may be woefully underestimated. Hypotension in patients with significant MR can be managed to a certain degree by manipulating heart rate and volume, but persistent hemodynamic instability may be best treated with inotropic support. Dobutamine,

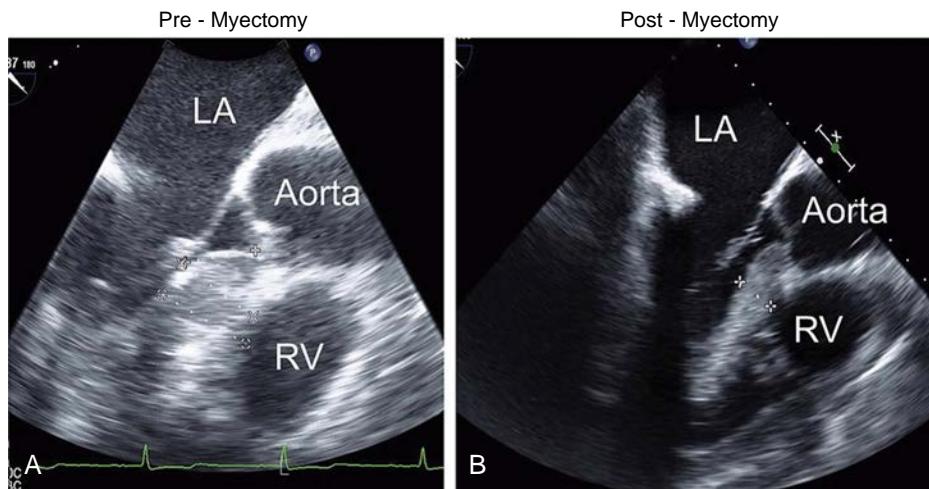


Fig. 54.35 Transesophageal echocardiography of septal measurements before myectomy (A) (thickness, 2.9 cm) and after myectomy (B) (thickness, 1.5 cm). LA, Left atrium; RV, right ventricle. (From Nagweh SF, Bierig SM, Budoff MJ, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with hypertrophic cardiomyopathy: endorsed by the American Society of Nuclear Cardiology, Society for Cardiovascular Magnetic Resonance, and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr*. 2011;24:473–498.)

low-dose epinephrine, and milrinone are all acceptable inotropic choices, depending on the clinician's interpretation of the monitor data.

With respect to SVR, the general rule of thumb for patients with MR is to decrease afterload so that forward CO is maximized. Adequate anesthetic depth, systemic vasodilators, inodilators, and at times mechanical reduction of afterload with an IABP may be clinical options, depending on the situation. Direct-acting α_1 -agonists increase SVR and blood pressure, lower heart rate, and may worsen the MR. Temporary use of small doses of ephedrine may be a better choice, after which inotropic support should be considered if a persistent need exists to augment pressure.

Both PAP and PVR may be elevated in patients with either acute or long-standing MR. Secondary changes in RV size and function may be important clinical considerations. Factors that may increase PVR and unfavorably load an already dysfunctional right ventricle (e.g., hypoxia, hypercarbia, and acidosis) should be remedied whenever possible.

Finally, in the patient with acute, severe MR and cardiogenic shock from ischemic rupture of a papillary muscle, pharmacologic support of the LV, often accompanied by mechanical support with IABP counterpulsation, may be necessary.

Hypertrophic Obstructive Cardiomyopathy and the Mitral Valve. Hypertrophic obstructive cardiomyopathy (HOCM) may result in dynamic valvular insufficiency, as well as LV outflow tract (LVOT) obstruction. In addition, surgical attempts to repair an incompetent mitral valve can create iatrogenic LVOT obstruction.

Classically, HOCM is a familial disease transmitted with autosomal dominant inheritance. Inheritance and phenotypic expressions are heterogeneous and vary in their manifestations. Some mutations in genes that code for cardiac sarcomere proteins can cause hypertrophy of segments of the ventricle. Septal involvement is common, but HOCM can involve other areas of the LV as well.³⁶² This disease is the most common cause of sudden death in young people, but it can also cause death and morbidity in older patients.

When the basal septum of the LV is affected, the LVOT can narrow (Fig. 54.35). Depending on the shape of the ventricle and the mitral valve, dynamic outflow tract obstruction can occur, paired with mitral valve insufficiency. As the outflow tract is narrowed by hypertrophy, the basal septum and the anterior leaflet of the mitral valve come into close proximity. The hypertrophy and the reduced septal–anterior leaflet distance can create a channel that narrows to the point of creating a pressure gradient across the outflow tract. This obstructed flow and its pressure gradient lead to progressive compensatory hypertrophy that, in turn, further narrows the outflow tract and worsens the gradient. As blood is ejected through this narrowed outflow channel during systole, the velocity of blood through the narrowed orifice increases. This increased blood velocity creates a Venturi effect that pulls the anterior leaflet of the mitral valve or the chordal structures into the outflow tract, thus leading to mechanical and dynamic obstruction of the LVOT and also causing MR because of a coaptation defect of the mitral valve.³⁶³ Echocardiographically, this is termed systolic anterior motion (SAM) of the mitral valve (Fig. 54.36). Such dysfunctional mitral valve motion is seen in cardiac surgical patients who present for surgical management of known HOCM (i.e., for surgical myectomy, mitral valve repair, or both).

Sometimes, SAM is noted preoperatively or as an incidental finding at the time of surgery in patients who present for surgical revascularization or mitral valve repair. Furthermore, SAM may be created iatrogenically as a result of surgical mitral valve repair. In patients with MR who are to undergo mitral valve repair, echocardiographic assessment and surgical inspection are performed to elucidate the mechanism of the mitral insufficiency. The patient may have ruptured or elongated chordal attachments, redundant or prolapsing leaflet tissue, or annular dilation that reduces effective leaflet coaptation. Frequently, multiple contributing factors are present. Surgical treatment can involve just a simple annuloplasty ring in the case of isolated annular dilation, but it more commonly involves resection of diseased segments of the mitral valve, possibly chordal reassignment or reconstruction, and a ring valvuloplasty.

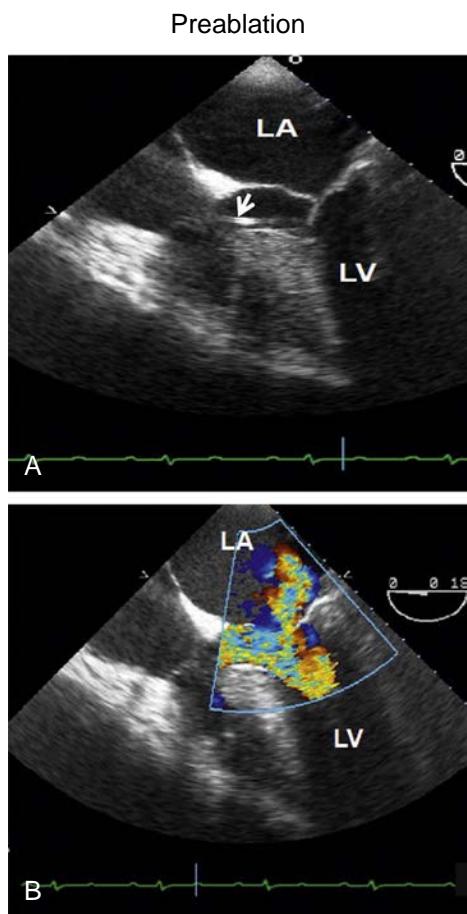


Fig. 54.36 Transesophageal echocardiographic images. (A) Two-dimensional image shows a narrowed left ventricular outflow tract with systolic anterior motion (arrow). (B) Color Doppler image shows high-velocity signals in mosaic color; eccentric mitral regurgitation is directed posterolaterally. LA, Left atrium; LV, left ventricle. (From Naguch SF, Bierig M, Budoff MJ, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with hypertrophic cardiomyopathy. *J Am Soc Echocardiogr*. 2011;24:473–498.)

Depending on LV geometry and size and the physical characteristics of the mitral valve, surgical repair may bring the anterior leaflet and the coaptation point of the valve into close approximation with the interventricular septum and the LVOT. That septal coaptation point can narrow enough to create a gradient in the outflow tract, so that the anterior leaflet is pulled into the LVOT by the Venturi effect, leading to obstruction and secondary mitral insufficiency (see Fig. 54.36). This anterior displacement of the mitral coaptation point and the amount of the extra anterior leaflet have been proposed to be mechanisms for SAM, thus leading to the development of surgical techniques that can reduce the incidence of SAM in high-risk patients.³⁶⁴ Anesthetic management of obstructive cardiomyopathy centers on fluid and pharmacologic interventions to decrease the magnitude of the obstruction and, at the same time, lessen the severity of the mitral insufficiency. Most patients with outflow tract abnormalities have normal to supranormal contractility.

Generally, inotropic agents should not be used. The thick, hypertrophied ventricle usually has reduced compliance

and is very load sensitive, so that outflow tract obstruction increases in hypovolemic conditions. Thus, optimizing preload and ventricular filling is appropriate both in managing the patient with LVOT and in assessing the need for surgical reconstruction of the LVOT, mitral valve repair, or both. Afterload reduction should be avoided because it worsens the obstruction. Conversely, increasing the afterload decreases the trans–outflow tract gradient and leads to a reduction of SAM and outflow tract obstruction. Hence, vasoconstrictors such as phenylephrine and vasopressin should be considered. In both congenital and iatrogenic LVOT obstruction, the degree of obstruction is dynamic. Obstruction is exacerbated by hypercontractile states and elevations in heart rate; therefore, reducing the heart rate with β -adrenergic blockade should be considered.

Continuous, skilled echocardiographic assessment and interpretation are important for optimal intraoperative management of these patients. Assessing the severity and mechanism of outflow tract obstruction and determining whether to reinstitute CPB to revise the repair or replace the valve are not innocuous decisions, and they must be carefully made jointly by the anesthesiologist and the surgeon, ideally with input from the appropriate cardiologist.

Minimally Invasive Mitral Valve Surgery. Cosgrove, Sabik, and Cohen were among the first surgeons to modify the traditional approach to cardiac surgery and pioneer the concept of minimally invasive cardiac surgery.³⁶⁵ The rapid development and refinement of minimally invasive techniques have resulted in the realizations that minimally invasive cardiac surgery does not compromise patients' safety or surgical exposure and that results are comparable to those of traditional open procedures. Mihaljevic and colleagues published a series of 1000 minimally invasive valve operations performed between 1996 and 2003, and noted the following benefits: reduced bypass and cross-clamp times, reduced stroke and MI rates, reduced length of hospital stay, and a higher rates of discharge home rather than to another facility.³⁶⁶

Access to the mitral valve through minimally invasive techniques can be through a lower hemisternotomy, a right parasternal incision excising the cartilaginous portions of the third and fourth ribs, or a right thoracotomy through a 4-cm incision.³⁶⁷ The mitral valve is then exposed through the left atrium or by a transseptal approach through the right atrium. Visualization of the valve for repair or replacement can be achieved in the following ways: by direct inspection and instrumentation; by "port access" under thoracoscopic guidance and video assistance; or by a more complete endoscopic technique using the DaVinci robotic system (Intuitive Surgical, Inc., Sunnyvale, CA). The DaVinci system uses robotic arms and instrumentation controlled by the surgeon sitting at a remote, computer-enhanced, three-dimensional imaging console to assist in completing the surgery.³⁶⁸ The DaVinci robot set up on the patient is shown in Fig. 54.37.³⁶⁹ Fig. 54.38 shows the surgeon's location in the operating room.³⁷⁰

Endoscopic or minimally invasive mitral procedures usually involve CPB with aortic and venous cannulas placed through the femoral artery and vein respectively. In addition, the surgeon may choose to use an endoscopic aortic occlusion device that allows a bloodless operative field

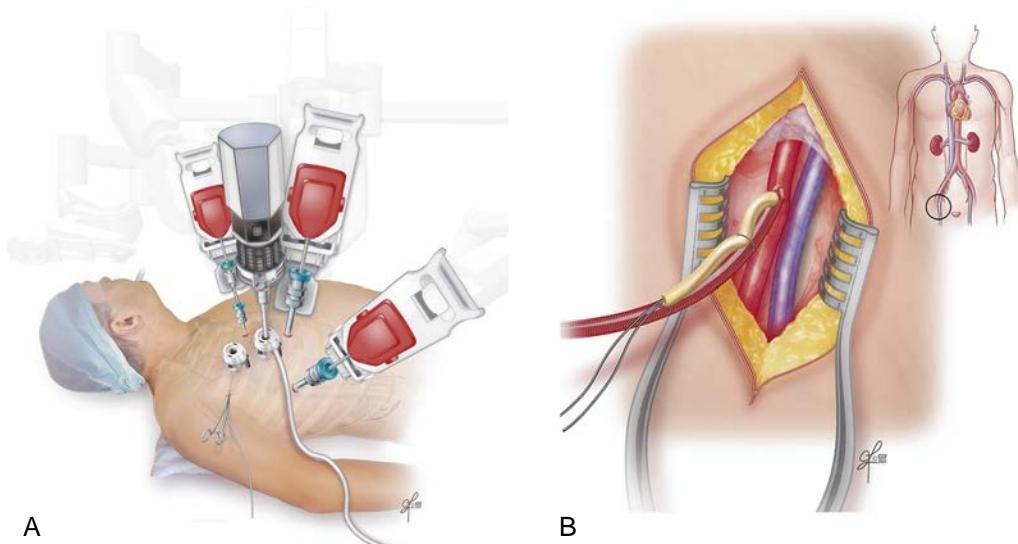


Fig. 54.37 Patient setup for robotic mitral valve repair. (A) Port placement; (B) cannulation of the femoral vessels. (Cleveland Clinic Foundation, 2017. From Cuartas M, Javadikasgari H, Pfannmueller B, et al. Mitral valve repair: robotic and other minimally invasive approaches. *Progr Cardiovasc Dis*. 2017;60[3]:394–404.)

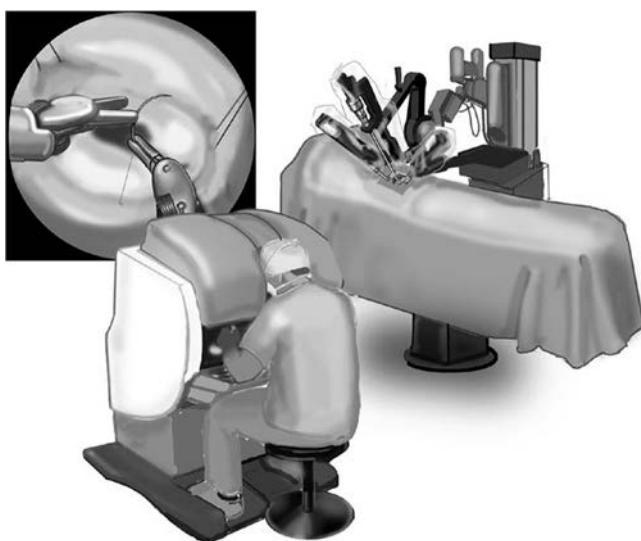


Fig. 54.38 Robotic surgery showing the DaVinci surgical system. The surgeon sits at the console and the robot is positioned at the operating table. The inset shows the surgeon's view of a mitral valve repair. (From Soltesz EG, Cohn LH. Minimally invasive valve surgery. *Cardiol Rev*. 2007;15:109–115.)

and the delivery of cardioplegia (Fig. 54.39).³⁷¹ As mentioned with total endoscopic coronary revascularization surgery, positioning of the EAOCB requires intraoperative fluoroscopy or echocardiography to confirm the catheter's position definitively. Known concerns and risks include catheter migration into the heart across the aortic valve and distal migration with occlusion of the brachiocephalic trunk.³⁷² Alternatively, the aorta can be occluded directly with flexible cross-clamps introduced through small chest wall incisions. The Chitwood transthoracic aortic cross-clamp (Scanlan International, Inc., St. Paul, MN) and the Cosgrove Flex Clamp (Cardinal Health, McGaw Park, IL) are being used for this purpose (Fig. 54.40).³⁶⁷ Cardioplegia needles may be inserted under direct vision or thoracoscopic

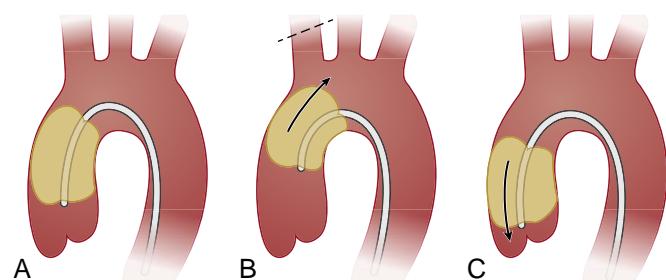


Fig. 54.39 (A) Drawing of a well-positioned EndoClamp in the ascending aorta. (B) Distal migration of the EndoClamp and potentially obstructing flow to the innominate artery. (C) Proximal migration of the EndoClamp that may prevent adequate aortic occlusion or cardioplegia. (Modified with permission from Kottnerberg-Assenmacher E, Kamler M, Peters J. Minimally invasive endoscopic port-access intracardiac surgery with one lung ventilation: impact on gas exchange and anaesthesia resources. *Anaesthesia*. 2007;62:231–238; and From Vernick WJ, Woo JY. Anesthetic considerations during minimally invasive mitral valve surgery. *Semin Cardiothorac Vasc Anesth*. 2012;16:11–24.)



Fig. 54.40 Chitwood transthoracic aortic cross-clamp (Scanlan International, Inc., St. Paul, MN) seen before use. (From Vernick WJ, Woo JY. Anesthetic considerations during minimally invasive mitral valve surgery. *Semin Cardiothorac Vasc Anesth*. 2012;16:11–24.)

guidance.³⁷² Retrograde cardioplegia, although not necessarily used in all patients, can be accomplished by directly cannulating the coronary sinus with a retrograde catheter at the operative site (RA approach) or by placing a percutaneous coronary sinus catheter in the internal jugular vein and positioning it under echocardiographic guidance.

Secondary operative considerations include the unique positioning of the patient for the use of robotic instrumentation. Most minimally invasive approaches require a 30-degree “right side up” position.

Anesthetic management includes selective lung ventilation with the use of a double-lumen tube or bronchial blocker, if this is needed for surgical exposure. Monitoring considerations are similar to those for standard approaches to valvular heart surgery. Furthermore, a PA ventilation (PA vent) catheter is placed in a manner similar to placement of a PA catheter.³⁷² These two catheters differ in two important ways. First, the PA vent has a significant amount of transducer “noise” in the tracings due to its excessive compliance. Second, the PA vent has fewer ports and thus does not allow for CO measurement. Some surgeons prefer to place a PA vent in the field. In these cases the cardiac anesthesiologist can place a PA catheter, and derive the benefits of mixed venous blood sampling and CO measurement in addition.

The outcomes of minimally invasive mitral valve surgery have been encouraging. Although prospective trials comparing minimally invasive mitral valve surgery and standard approaches are limited, developments in technology and an integrated team approach may facilitate favorable postoperative outcomes.³⁶⁷ Reports describe mortality and morbidity rates comparable to those of full-sternotomy approaches, with reduced postoperative bleeding and trends toward reduced length of hospital stay and a higher rate of discharge home.^{370,373}

Aortic Valve Disease

Aortic Stenosis

PATHOPHYSIOLOGY. AS is the most common cardiac valve lesion diagnosed in the United States. Marked increases in the annual volume of aortic valve replacements have occurred recently, especially in older and high-risk patients.³⁷⁴

AS is often caused by congenital defects in the valve because congenital bicuspid aortic valve occurs in 1% to 2% of the population.³⁷⁴ Inheritance has been found to play a role, with an autosomal dominant pattern and a variable penetrance.³⁷⁵ Even a normally functioning bicuspid aortic valve tends to open and close with abnormal folding and creasing, leading to scarring and calcification which ultimately culminates in AS with or without aortic regurgitation (AR). Although patients with a bicuspid aortic valve are asymptomatic until late in the disease process, severe, symptomatic AS or AR may develop in midlife. In addition, the abnormal motion of the bicuspid leaflets causes some turbulent flow into the aorta, which eventually can lead to dilatation and subsequent rupture or dissection.^{376,377} A typical “fish-mouth” or elliptical shaped opening of the aortic valve in a midesophageal, cross-sectional TEE view of the valve is a telltale sign of a bicuspid aortic valve.

Acquired AS is usually the result of senile degeneration with sclerosis and calcification of the valve. The prevalence of AS in the population is increasing. Approximately 3% of people over the age of 75 years have AS, and 12% of these have moderate or severe aortic stenosis.^{374,378} A clear association is reported between clinical risk factors for atherosclerotic disease (e.g., the process of chronic inflammation)

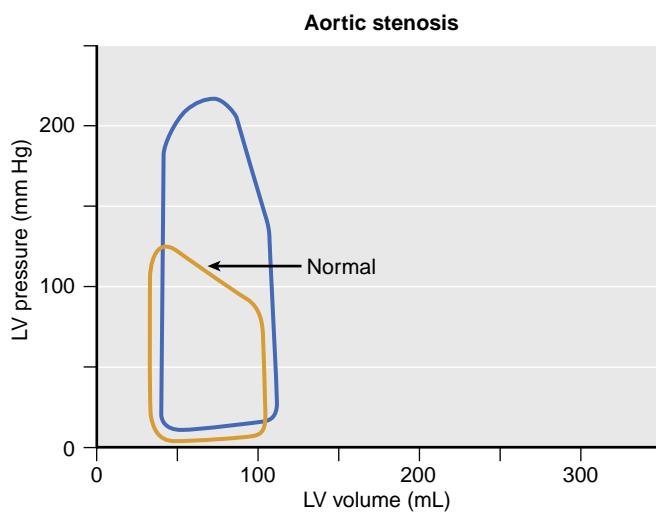


Fig. 54.41 Pressure-volume loop in aortic stenosis. LV, Left ventricular. (Modified from Jackson JM, Thomas SJ, Lowenstein E. Anesthetic management of patients with valvular heart disease. *Semin Anesth*. 1982;1:239.)

and the development of AS.^{378,379} In developed countries, rheumatic disease is a less common cause of AS, and AS is usually associated with concomitant AR.

A typical pressure-volume loop for AS is shown in Fig. 54.41. In patients with AS, the obstruction of LV outflow increases peak systolic wall stress, resulting in chronic pressure overload that directly stimulates parallel replication of sarcomeres in the LV and consequently causes concentric ventricular hypertrophy. The peak pressure generated by the LV during systole is much higher than normal because of the high transvalvular pressure gradient. Concentric LV hypertrophy nearly always develops as a result of the increases in pressure load (Fig. 54.42). This increased load also leads to diastolic dysfunction, an increase in LVEDP, and subendocardial ischemia.

Echocardiography and intraoperative TEE in particular play important roles in the diagnosis and ultimate management of patients with AS, both in the outpatient setting and during surgical aortic valve replacement. The severity of AS can be assessed from various echocardiographic parameters. One that is commonly used is the aortic valve area (AVA). The normal range of the AVA is 3 to 4 cm²; AS is graded as severe if the AVA is reduced to 1 cm² or less.³⁸⁰ Another parameter commonly used to determine the severity of AS is the gradient across the aortic valve; AS is considered severe if the mean gradient is greater than 40 mm Hg.³⁵⁵ Echocardiography can be used to examine multiple aspects of the pathophysiology of AS, including the severity of AS, any structural abnormalities of the valve causing LVOT obstruction, any ascending aortic pathology, and any concomitant heart valve lesions.

With TEE, the best views for evaluating the aortic valve are the midesophageal aortic valve short-axis view, the midesophageal long-axis view, and the transgastric views. Midesophageal views are helpful in ascertaining the shape of the aortic valve and the two-dimensional anatomy of AS (Fig. 54.43), whereas transgastric views are helpful in obtaining gradient measurements across the valve and the LVOT (Fig. 54.44). In addition, both the midesophageal and

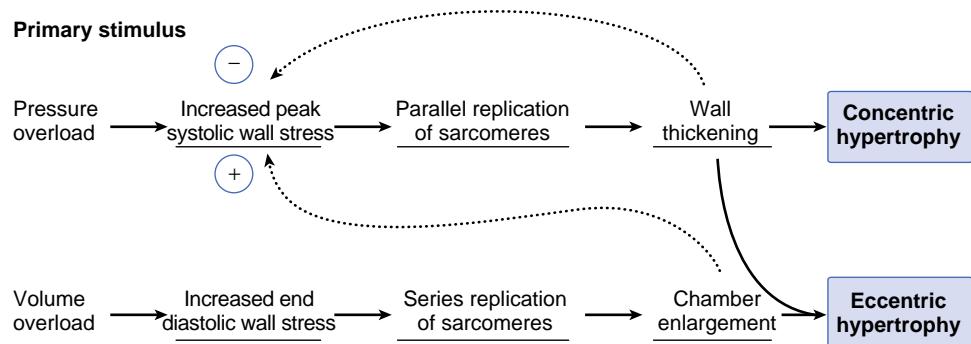


Fig. 54.42 The increased peak systolic wall stress resulting from chronic pressure overload directly stimulates concentric ventricular hypertrophy, which tends to counteract or “normalize” the elevated ventricular wall stress. (From Grossman W, Jones D, McLaurin LP. Wall stress and pattern of hypertrophy in the human left ventricle. *J Clin Invest*. 1975;56:56.)

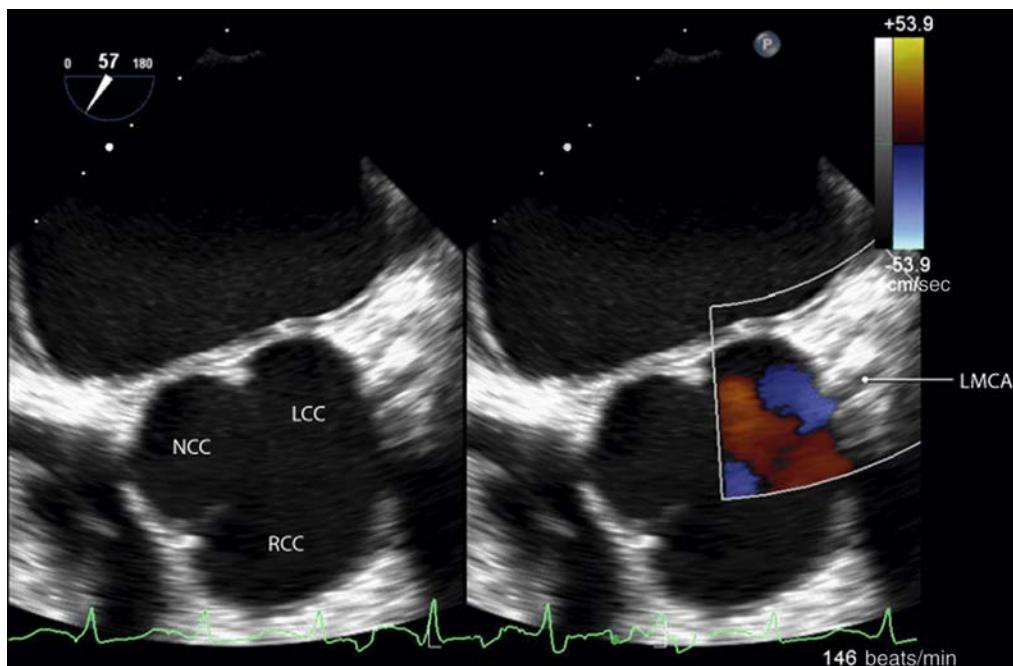


Fig. 54.43 Midesophageal aortic short-axis view. LCC, Left coronary cusp; LMCA, left main coronary artery; NCC, noncoronary cusp; RCC, right coronary cusp. (From Virtual TEE: <http://pie.med.utoronto.ca/tee>.)

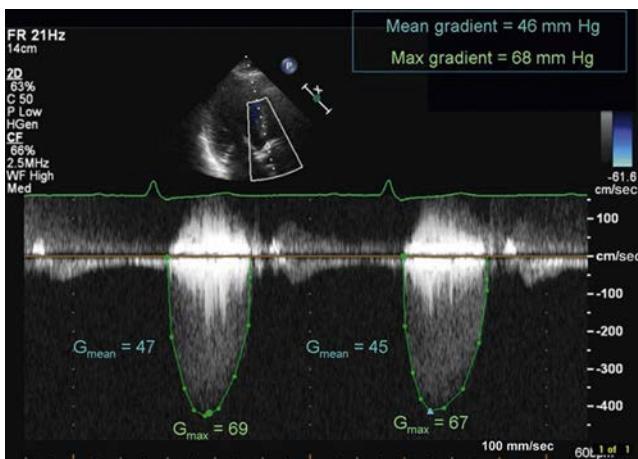


Fig. 54.44 Quantification of the degree of aortic stenosis with continuous Doppler. G_{max} , Maximum gradient; G_{mean} , mean gradient. (From http://web.stanford.edu/group/ccm_ecochardio/cgi-bin/media_wiki/index.php/Aortic_stenosis_assessment. Accessed August 21, 2014.)

the transgastric views can be used to measure the dimensions of the aortic valve annulus and the LVOT; these measurements are helpful in making surgical decisions related to the size of the valve.

Patients with AS who have not yet developed symptoms should be closely monitored over time for progression of the disease. Patients who develop symptoms (including decreased exercise tolerance and exertional dyspnea, angina, CHF, and syncope) are considered for valve replacement. A delay in surgical intervention in symptomatic patients can worsen their prognosis.³⁷⁸

Anesthetic Management. Premedication may alleviate a patient’s anxiety regarding cardiac surgery, and it helps to prevent perioperative tachycardia in patients with AS. Monitoring in these patients includes standard noninvasive modalities and invasive monitoring of blood pressure and CVP. Depending on the severity of the AS, pulse pressure may be as low as 50 mm Hg or less. TEE is indicated for

monitoring and the measurements obtained yield extremely valuable information (Fig. 54.45; see also Figs. 54.43 and 54.44).^{381,382}

Insertion of a PA catheter may be considered to monitor PAP and CO during surgical procedures, but is rarely needed in patients with normal ventricular function. Patients with AS are at increased risk if arrhythmias develop during PA catheter placement as coronary perfusion can be severely compromised. Furthermore, if cardiopulmonary resuscitation is needed, chest compressions do not generate effective CO across the stenotic valve.

The anesthetic management of patients with AS should not involve any medication that could have negative inotropic, tachycardic, or vasodilatory effects. Furthermore, every effort should be made to ensure that the patient stays in sinus rhythm. In patients with AS, the atrial kick may contribute as much as 40% of the total CO.

Table 54.19 summarizes the goals of anesthetic care of a patient with AS.

Aortic Regurgitation

PATHOPHYSIOLOGY. AR is the flow of blood from the aorta backward into the LV during the diastolic phase of the cardiac cycle. Chronic AR is more prevalent than acute AR and has compensatory physiologic changes, whereas acute AR is not handled well hemodynamically. However, the precise prevalence of AR—acute and chronic—remains unknown.³⁸³

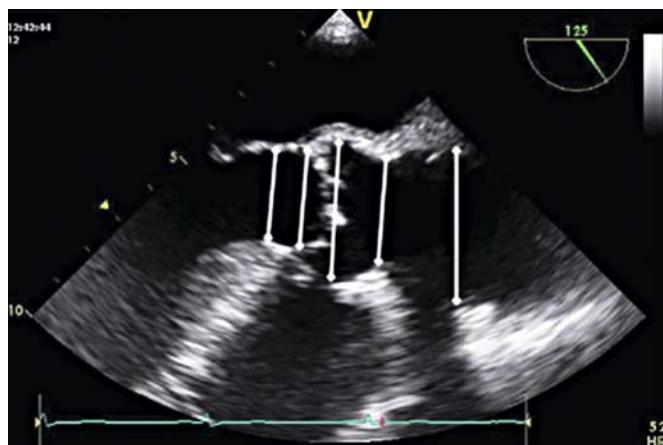


Fig. 54.45 Intraoperative transesophageal echocardiographic measurements of the aortic valve annulus, including the diameter of the left ventricular outflow tract (to exclude severe asymmetric septal hypertrophy), aortic valve annulus, sinuses of Valsalva, sinotubular junction, and ascending aorta (arrows, from left to right). (From Pasic M, Buz S, Dreyssse S, et al. Transapical aortic valve implantation in 194 patients: problems, complications, and solutions. *Ann Thorac Surg*. 2010;90:1463–1469; discussion: 1469–1470.)

Causes of chronic AR include congenital lesions, degenerative processes, and rheumatic disease, but idiopathic causes seem to be the most common.³⁸³ These processes cause malcoaptation of the aortic valve leaflets by producing abnormalities in the leaflets themselves or dilation of the aortic valve annulus, the aortic root, or both. Abnormalities of the aortic valve leaflets include congenital conditions (e.g., bicuspid aortic valve), endocarditis, rheumatic heart disease, inflammatory diseases, certain connective tissue diseases, and chest wall trauma causing injury to an aortic valve leaflet. Dilation of the proximal aortic root may be caused by annuloaortic ectasia resulting from long-term chronic hypertension or simply from the normal aging process.³⁸⁴ Other aortic valve annular or aortic root causes of AR include Marfan syndrome, syphilis, congenital diseases such as osteogenesis imperfecta and Ehlers-Danlos syndrome, and idiopathic causes.^{383,384}

CHRONIC AORTIC REGURGITATION. Patients with chronic AR may remain asymptomatic for years or even decades. The LV undergoes a process of remodeling resulting from series replication of sarcomeres and the development of eccentric ventricular hypertrophy and chamber enlargement in the presence of a chronically increasing volume of regurgitation (see Fig. 54.42). Although the pressure-volume loop is shifted far to the right in patients with chronic AR, the LVEDP remains relatively normal because the LVEDV increases slowly (Fig. 54.46). Forward flow is improved by peripheral vasodilation. Typically, a normal EF is maintained by a large stroke volume. However, over time, increases in LV wall stress and afterload result. Eventually, as LV dilation and hypertrophy progress, irreversible LV dysfunction develops, and patients become symptomatic. As a compensatory mechanism for poor CO, sympathetic constriction of the peripheral vasculature occurs to maintain blood pressure, but this adaptation exacerbates regurgitation and further reduces CO.

In addition to a detailed history and physical examination, diagnostic modalities such as magnetic resonance imaging, radionuclide angiography, and exercise stress testing are used to assess AR. However, echocardiography remains the most important diagnostic tool (Fig. 54.47). The severity of AR is assessed as follows: regurgitation of less than 20% of the total LV stroke volume is considered mild, 20% to 39% is considered moderate, 40% to 60% is considered moderately severe, and more than 60% is considered severe.

Several semiquantitative echocardiographic modalities are used to assess AR. These include color flow mapping, in which the ratio of the AR jet width to the width of the LVOT is used to ascertain the severity of the condition. Jets that appear to be central in flow may appear to be larger than

TABLE 54.19 Pathophysiologic Changes Associated With Aortic Stenosis

LV Preload	Heart Rate	Contractility	Systemic Vascular Resistance	Pulmonary Vascular Resistance
Aortic stenosis	↑	↓ (sinus)	Maintain constant	↑

LV, Left ventricular.

From Townsley MM, Martin DE. Anesthetic management for the surgical treatment of valvular heart disease. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:327.

they actually are because of the entrainment of fluids.³⁸³ This possibility should be considered when one is evaluating a centrally directed jet as compared with an eccentrically directed jet. The vena contracta, the narrowest part of the regurgitant jet, can be measured to determine the severity of AR (see Fig. 54.47). A vena contracta measurement of 6 mm or greater carries a sensitivity of 95% and a specificity of 90% for the presence of severe AR.³⁸⁵ A vena contracta

of less than 3 mm indicates mild AR. The pressure half-time of the AR jet can be measured echocardiographically. A pressure half-time of less than 200 ms indicates severe AR, while a pressure half-time of greater than 500 ms indicates mild AR. In addition, holodiastolic flow reversal in the descending aorta signifies moderate-to-severe AR.

Although patients with chronic AR can remain asymptomatic for decades, symptoms of left-sided HF eventually occur, such as exercise intolerance, dyspnea, and paroxysmal nocturnal dyspnea or orthopnea. Afterload reduction may become necessary as the disease progresses. In addition, a few patients present with angina despite having normal coronary arteries; this angina results from poor coronary perfusion resulting from low diastolic aortic pressure. A difficult decision for the cardiologist is at what point in the course of the disease surgery should be performed to prevent the development of irreversible LV dysfunction, especially in patients with severe chronic AR.^{382,383}

ACUTE AORTIC REGURGITATION. Acute AR is less common than chronic AR but carries a more ominous prognosis. Common causes of acute AR include trauma, bacterial endocarditis, and aortic dissection. Rarely, acute AR occurs as an idiopathic complication, such as after aortic valvuloplasty. The pathophysiology of acute AR is that an acute volume load compromises the LV. Because the LV has not had time to undergo the process of eccentric hypertrophy, as it does in chronic AR, it is unprepared to accommodate this sudden increase in volume. As shown in Fig. 54.46, this sudden increase in the LVEDP causes a rightward shift in the pressure-volume loop.³⁸⁴ A sympathetic response is activated; tachycardia and an increased contractile state are the chief compensatory mechanisms for maintaining adequate CO. Unless acute AR is managed appropriately, these compensatory mechanisms rapidly fail. Furthermore, the sympathetic response causes sympathetic constriction of the peripheral vasculature, thereby increasing SVR and further worsening the AR. LV function can deteriorate rapidly, necessitating emergency surgery. Vasodilator therapy may temporarily stabilize the patient during transport to the operating room.³⁸³

ANESTHETIC MANAGEMENT. The anesthetic management of patients with AR should include maintaining a relatively fast heart rate (≈ 90 beats/min) and a relatively low SVR while maintaining preload and contractility. Table 54.20 summarizes the goals of anesthetic care for a patient with AR. Light premedication is recommended. Regarding the choice of drugs for general anesthesia in these patients, medications that cause bradycardia or high blood pressure should be avoided because these changes worsen the degree of AR and can precipitate LV failure.

Preoperative placement of an arterial catheter and central venous catheter is standard, and a PA catheter may

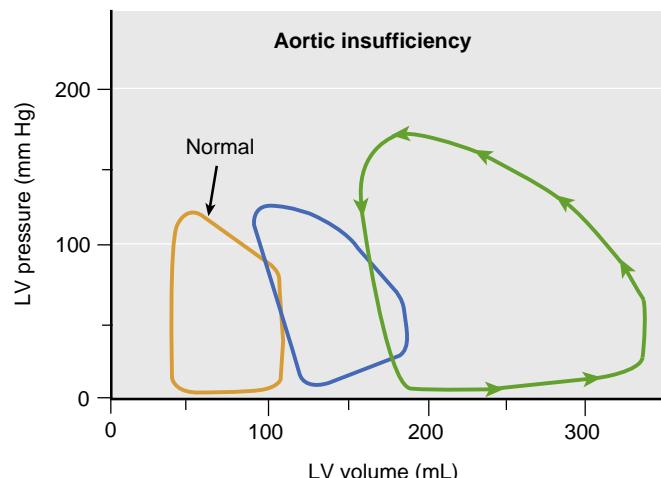


Fig. 54.46 Pressure-volume loop in aortic regurgitation (AR). Acute AR, middle loop; chronic AR, right loop. LV, Left ventricular. (Modified from Jackson JM, Thomas SJ, Lowenstein E. Anesthetic management of patients with valvular heart disease. *Semin Anesth*. 1982;1:239.)



Fig. 54.47 Vena contracta. Calipers measure the narrowest portion of the aortic regurgitant jet, which corresponds to an approximation of the regurgitant orifice area. Ao, Aorta; LA, left atrium; LV, left ventricle. (From Perino AC, Reeves ST, eds. *A Practical Approach to Transesophageal Echocardiography*. 2nd ed. Philadelphia; Lippincott Williams & Wilkins; 2008:232.)

TABLE 54.20 Pathophysiologic Changes Associated With Aortic Regurgitation

	LV Preload	Heart Rate	Contractility	Systemic Vascular Resistance	Pulmonary Vascular Resistance
Aortic regurgitation	↑	↑	Maintain	↓	Maintain

LV, Left ventricular.

From Townsley MM, Martin DE. Anesthetic management for the surgical treatment of valvular heart disease. In: Hensley FA, Martin DE, Gravlee GP, eds. *A Practical Approach to Cardiac Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2013:335.

be considered if PAPs are high or ventricular function is compromised. In the prebypass period, TEE allows the anesthesiologist to determine the cause and severity of the AR, evaluate LV size and function, and assess the function of the other cardiac valves. Furthermore, TEE assessment in the immediate postbypass period confirms the proper positioning and function of the new aortic valve.

Weaning from CPB may be complicated by preexisting LV dysfunction. Furthermore, mechanical aortic valve replacement results in a mild transvalvular pressure gradient. Therefore, inotropic agents may be needed to improve LV function. Preload augmentation must be continued to maintain the filling of the dilated LV.

Minimally Invasive Aortic Valve Surgery. The surgical approach to the aortic valve can be made through several different incisions, including a right parasternal incision, upper hemisternotomy, or lower hemisternotomy.³⁶⁵ Because surgical exposure is limited, transcutaneous defibrillator pads should be placed before preparing and draping, should the need to defibrillate arise.³⁷²

Placement of CPB cannulas from distant sites is a hallmark of minimally invasive surgery and speaks to the importance of TEE guidance led by the anesthesiologist. To achieve arterial access, a surgical decision may be made to cannulate the femoral artery.³⁷³ Alternatively, if aortic atherosomatous disease precludes retrograde aortic arterial flow, the surgeon may attempt aortic cannulation through an incision directly into the aorta, or through the axillary artery.^{370,372} Venous bypass drainage can be accomplished by cannulating the right atrium (if surgical exposure is not compromised) or through the femoral vein. Positioning of the distal drainage portion of the femoral vein cannula in the IVC, right atrium, or distal segment of the SVC is guided and confirmed by TEE (Fig. 54.48).³⁷³ To reduce the incidence and magnitude of retained intracavitory LV air, carbon dioxide can be insufflated into the surgical field.³⁷⁰

In general, anesthetic monitoring considerations are similar to those for standard approaches to valvular heart surgery. However, in the absence of direct visualization of the heart, TEE is even more valuable for assessing cannula positioning and ensuring adequate ventricular de-airing.³⁷² If retrograde cardioplegia is required, TEE may

be used to guide a transjugular retrograde catheter into the coronary sinus.

One report of a large series of minimally invasive aortic valve procedures included more than 900 patients. Compared with the national average, these patients had decreased blood product use (with 53% of first-time aortic valve surgery patients receiving no blood products) and higher rates of discharge home (including 40% of the octogenarian patients).³⁸⁶

Other Valvular Disease

Tricuspid Valve Disease. Right-sided valvular disease in adults is most often a manifestation of increased pulmonary pressures (e.g., secondary to intrinsic lung disease, pulmonary vascular disease, or left-sided cardiac disease), but it can also result from rheumatic, traumatic, infectious, humoral, and/or neoplastic processes.

Tricuspid Regurgitation. Tricuspid valvular disease in adults is predominately regurgitant. Though it may be well-tolerated when mild-moderate, patients with significant TR will eventually demonstrate signs and symptoms of elevated RA pressure (e.g., hepatomegaly, peripheral edema, ascites). Compensatory changes with long-standing TR involve RV and RA chamber dilatation, and possibly atrial fibrillation. Long-standing TR and RV enlargement will progressively result in RV systolic dysfunction due to the alteration in RV geometry, which leads to further tricuspid annular dilation, worsening of TR severity, and further RV enlargement. TR has been categorized into stages based on severity and secondary findings of importance with implications regarding the manner of repair once indicated.³⁸⁷

- Stage 1: initial annular dilatation secondary to RV enlargement. TR is not usually significant.
- Stage 2: progressive annular dilatation results in poor leaflet coaptation. TR is significant. RV dilatation is more pronounced.
- Stage 3: severe RV dilatation and dysfunction, with tethering of tricuspid leaflets due to RV dilatation causing severe TR

If the tricuspid insufficiency is secondary to RV pressure overload states, as with pulmonary hypertension, RV hypertrophy also ensues. This hypertrophy and increased RV pressure can lead to leftward displacement of the interventricular septum and impaired LV systolic and diastolic performance.

Primary or structural TR results in morphological abnormalities of the leaflets themselves as a result of rheumatic, traumatic, infectious, humoral, and/or neoplastic processes. Secondary or functional TR is the most commonly observed etiology of TR in Western countries,³⁸⁸ and can be a sequelae of left-sided cardiac disease that results in elevated pulmonary vascular pressures, cor pulmonale, and/or primary pulmonary hypertension. Functional TR is most often the result of a dilated tricuspid annulus (the tricuspid leaflets are morphologically normal), and is frequently present in patients undergoing aortic, and particularly mitral, valve surgery. It has long been known that a small degree of TR can be demonstrated in about 70% of

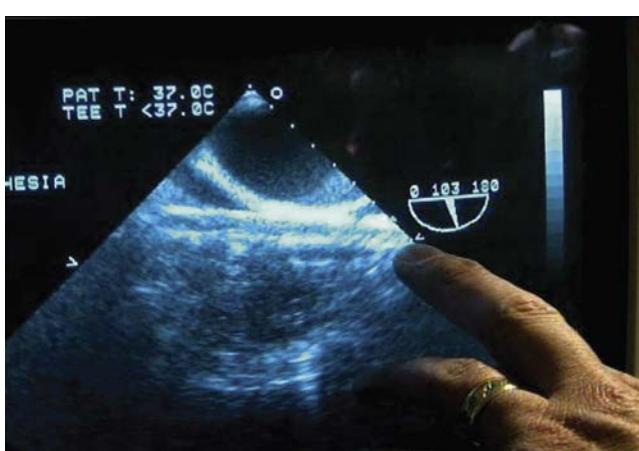


Fig. 54.48 Venous cannula placement through the inferior vena cava—right atrium into the superior vena cava.

normal individuals, but it remains somewhat controversial to conclude that it is therefore normal to have TR. What is not in debate, however, is that TR leads to progressive right-sided volume overload and progressive annular dilatation that will not spontaneously remodel following repair of left-sided valvular lesions, and may even continue to dilate further.³⁸⁹

Severe TR is a predictor of long-term mortality (65% 1-year survival rate in patients with severe TR compared with 90% of patients without TR),³⁹⁰ and thus is now considered a class I indication in both American and European guidelines for concomitant tricuspid valve repair or replacement in patients undergoing left-sided heart valve surgical procedures. Tricuspid annular dilatation alone with lesser degrees of TR is considered a class II indication for tricuspid valve repair or replacement in patients undergoing left-sided heart valve surgical procedures.

TR impairs the ability of the RV to pump blood through the lungs and across to the left side, so the main anesthetic management consideration for the patient with TR is preload preservation. The most effective management strategy to improve forward flow from the RV derives from the principle of ventriculoarterial coupling, which holds that no matter how compromised the intrinsic systolic mechanics of a pumping chamber may be, its ability to function as a pump will generally be improved by reducing the afterload against which it must pump. Thus, reductions in PVR (e.g., with nitric oxide or inhaled prostaglandins) can help to optimize RV function, decrease TR, and get blood across the pulmonary bed to the left side. High-normal heart rates, maintenance of atrial kick, and judicious use of inotropes or inodilators will also help optimize forward flow from the RV as needed. Repair of functional TR usually entails either surgical annuloplasty (e.g., with a ring or band) or bicuspidization, either of which are usually successful in decreasing the amount of TR, but which can sometimes leave mild residual TR or create an elevated pressure gradient across the tricuspid valve if the annular size is excessively downsized.³⁸⁵

TRICUSPID STENOSIS. Tricuspid stenosis (TS) is a relatively rare clinical finding in adults. Patients with TS may have significant RA enlargement and possibly atrial fibrillation. Chronic elevation of RA pressure leads to IVC dilatation, jugular venous distention, and hepatic congestion. Clinical symptoms and signs can include hepatomegaly (with or without hepatic dysfunction), ascites, peripheral edema, fatigue, and dyspnea.^{385,391}

TS results in reduced RV filling. The normal tricuspid valve area is 7 cm², and ventricular filling is compromised once the valve area falls to less than 1.5 cm². The severity of TS is usually assessed echocardiographically by measuring the Doppler-derived transvalvular gradient. Mild TS is associated with a gradient of 2 mm Hg or less; moderate TS, 2 to 6 mm Hg; and severe TS, greater than 6 mm Hg.³⁹²

Anesthetic management centers on maintaining preload and controlling heart rate. Overt tachycardia should be avoided because it significantly shortens the interval for diastolic filling, which is necessary in these patients. The target heart rate is not frank bradycardia, because CO may not be optimal, but the heart rate should be in the low-normal range. When atrial fibrillation is not part of the clinical picture, preserving AV synchrony is important

for maintaining RV preload and CO. Although RV inotropic failure is not usually a major concern in isolated TS, it may be when TS is a part of multivalvular heart disease or ischemic heart disease, thus warranting consideration of inotropic support. SVR should be maintained because the fixed obstruction at the level of the tricuspid valve prevents a compensatory increase in preload if afterload declines.

Pulmonic Valve Disease. Pulmonic valvular disease can be congenital or acquired, with congenital etiologies responsible for the vast majority of the cases. Previous pulmonic valve surgery is not an infrequent etiology of pulmonic valve disease in adults.

PULMONIC STENOSIS. Pulmonic stenosis (PS) as an entity entails an obstruction to right-sided CO, with the obstruction potentially located at the subvalvar level (just below the valve in the RVOT), at the level of the valve itself, or supravalvar (above the valve in the main PA). Valvular PS is caused by congenital valve abnormalities in 95% of cases,³⁸⁵ but isolated valvular PS is relatively rare as a congenital lesion. Acquired etiologies in adults include carcinoid disease, rheumatic disease, and prior pulmonic valve, RVOT, or main PA procedures. This would include a prior Ross Procedure (to correct congenital AS) in which the pulmonic valve is translocated to the aortic position and a homograft is implanted in the pulmonic position. Elevated transvalvular pressure gradients may lead to RV hypertrophy, RV and tricuspid annular dilatation, TR, and possibly eventual RV failure. Treatments for valvular PS include percutaneous balloon valvuloplasty, surgical valvotomy, RV to PA conduits, and surgical or percutaneous valve replacement. However, recent data indicate that the currently available percutaneous transcatheter pulmonic valve "may not be able to adequately address a subset of patients with complex RVOT morphology."³⁹³ Medical management strategies for valvular PS include judicious heart rate control, preload maintenance, and inotropic support as a bridge to percutaneous or surgical intervention. Supravalvular narrowings are often amenable to percutaneous dilatation and/or stenting. Subvalvular muscular infundibular obstruction may occur naturally in tetralogy of Fallot (and is generally relieved by afterload augmentation with or without volume loading as needed). Infundibular obstruction can also result from chronic long-standing PS. As with dynamic LVOT obstruction, tachycardia and hypovolemia can precipitate a dynamic clinical condition in which RVOT obstruction is accentuated. Dynamic RVOT obstruction is managed as for dynamic LVOT obstruction, with preload maintenance, afterload augmentation, control of heart rate, and avoidance of an enhanced inotropic state.

PULMONIC INSUFFICIENCY. Pulmonic insufficiency (PI) can result when the pulmonic valve is rendered incompetent in childhood during balloon valvuloplasty for congenital PS or during surgical valvotomy for tetralogy of Fallot. PI may also be associated with rheumatic heart disease, pulmonary hypertension, pulmonary embolus, carcinoid syndrome, trauma, Marfan syndrome, idiopathic dilation of the pulmonary trunk, and endocarditis.³⁸⁵ A common cause of mild PI is left-sided disease resulting in pulmonary hypertension. Most patients are asymptomatic, but long-standing severe PI can lead to symptomatic RV dilation and failure, warranting replacement of the pulmonic valve.

Anesthetic management requires being mindful of the primary cardiac or pulmonary disease that led to the pulmonic valvular insufficiency. In primary PI, anesthetic management goals may include maintaining preload, supporting contractility, and reducing PVR through ventilatory maneuvers and/or initiation of selective pulmonary vasodilatation (e.g., with nitric oxide or inhaled prostaglandins).

Minimally invasive surgical approaches can also be used to treat tricuspid valve disease,³⁹⁴ as well as ASDs. Minimally invasive approaches to heart surgery are best accomplished through careful design of a hybrid operating room.

Structural Heart Procedures

Hybrid Operating Room. To address the technologic and procedural demands regarding surgical and imaging equipment for selected endovascular and transcatheter procedures, hybrid operating rooms have been built in many institutions. These rooms have complete dual capabilities for procedures that require fluoroscopy, open surgery, or both. Ideally, such rooms are within or adjacent to the regular surgical suite. The physical location of such hybrid rooms may represent an advance in care in that key personnel are more readily available to handle unanticipated complications and emergencies.

The types of procedures that are performed in the hybrid operating room vary according to institutional preferences but may include (1) electrophysiology procedures, (2) percutaneous management of valvular lesions, (3) placement of occlusion or umbrella devices to close intracardiac defects or communications, (4) placement of percutaneous VAD, (5) left atrial appendage (LAA) occlusion device placement, and (6) stenting of abdominal or thoracic aortic aneurysms.³⁹⁵⁻³⁹⁷

Although requirements vary depending on the nature of the procedure, sedation or general anesthesia along with monitoring by an anesthesiologist improves the efficacy and safety of many procedures.³⁹⁸ Providing stable hemodynamics for organ perfusion and preservation during the procedure is an important goal. Some procedures can be performed with the aid of monitored anesthesia care or regional blocks, provided a certain patient comfort level can be achieved; however, in many cases, a general anesthetic regimen may be the best option. If indicated, general anesthesia with endotracheal intubation provides a controlled situation: the patient's comfort is maximized, and the airway is secured.³⁹⁹ Use of a laryngeal mask or a standard mask airway is also possible, but the constant diaphragmatic movements that occur during spontaneous ventilation may interfere with fluoroscopic visualization of cardiac and vascular structures. In the absence of significant complications or comorbid conditions, the patient may be allowed to emerge from anesthesia before being transferred to a recovery area. In more complex cases, the patient may be transferred to an ICU and a slower emergence from general anesthesia can take place.

Most percutaneous procedures that are performed with fluoroscopic and TEE guidance are performed with the patient under general anesthesia. These include mitral valve repairs and many TAVI procedures where sternotomy

and CPB are avoided, yet TEE is crucial to the performance and evaluation of the procedure.³⁹⁶ Percutaneous closure devices, such as for ASDs and VSDs, and fenestrations are often performed with intracardiac echocardiography (ICE). If ICE or transthoracic imaging can be used, or imaging can be restricted to fluoroscopy only, procedures can be done with sedation.^{397,398} Large-bore peripheral or femoral venous access is needed, and a radial arterial line is often placed.

Percutaneous VADs (TandemHeart, Cardiac Assist, Inc., Pittsburgh, PA, and Impella Recover LP 2.5 and 5.0, Abiomed, Inc., Danvers, MA) are placed in patients undergoing high-risk coronary interventions or ablation procedures or who are in cardiogenic shock.³⁹⁷ These devices can almost fully support LV function and produce a CO with nonpulsatile blood flow. Thus, pulse oximetry and noninvasive blood pressure measurement may not work properly, and intraarterial line placement is recommended. Either sedation or general anesthesia can be used, depending on the patient's hemodynamic status and ability to cooperate. Large-bore intravenous access is desirable because a large amount of blood loss is possible. Surgical backup is necessary during these procedures.

Transcatheter Aortic Valve Implantation. Symptomatic patients with severe AS have a poor prognosis; the mortality at 1 year in medically treated patients is 50%.⁴⁰⁰ Transcatheter aortic valve implantation (TAVI) was originally an alternative treatment option in patients with severe AS for whom cardiac surgery and traditional aortic valve replacement posed substantial risks, particularly patients of advanced age who have extreme comorbidities (e.g., porcelain aorta, prior radiation therapy, frailty, severe hepatic or pulmonary disease).⁴⁰¹⁻⁴⁰³ Now transcatheter aortic valve replacement is being employed for treatment of patients categorized as moderate-risk patients, and trials are under way to study the procedure in low-risk patients.⁴⁰⁴

The technologic advances made in the development of TAVI procedures are ingenious. However, the procedure is associated with short-term and long-term morbidity, including mortality, stroke, need for permanent pacemaker insertion, vascular complications, valve embolization, renal failure, cardiac rupture, aortic rupture, cardiac tamponade, and bleeding.^{405,406} Published guidelines regarding the TAVI procedure recommend specialized multidisciplinary heart teams that include cardiologists, cardiac surgeons, anesthesiologists, intensivists, nurses, and others.⁴⁰⁴ The hybrid operating room or cardiac catheterization laboratory (CCL) where the procedure is performed must have adequate space, expert echocardiography, emergency supplies, support from colleagues, and immediate access to CPB technicians and a cardiac surgeon if necessary.

The TAVI procedure requires vascular access to the aortic valve annulus (Fig. 54.49).⁴⁰⁷ Most procedures are performed using retrograde access via the femoral artery, however, other retrograde access can be accomplished using the subclavian or innominate artery or a direct ascending aortic approach. In cases where aortic disease or anatomy precludes a retrograde approach, anterograde access can also be performed through surgical exposure of