CHAPTER 4

Cardiac Anesthesia

4 Cardiac Anesthesia

Although excellence in pre- and postoperative care can often make the difference between an uneventful and a complicated recovery, the care provided in the operating room usually has the most significant impact on patient outcome. Performing a technically proficient, complete, and expeditious operation is only one component of this phase. Refinements in anesthetic techniques and monitoring, cardiopulmonary bypass (CPB), and myocardial protection have enabled surgeons to operate successfully on extremely ill patients with far advanced cardiac disease and multiple comorbidities. Use of off-pump modalities to avoid CPB is particularly useful in patients at high risk because of associated morbidities. Many patients, previously considered inoperable, will now survive the operative period to provide a challenge to postoperative care. This chapter will describe anesthesia considerations in cardiac surgery, including monitoring, transesophageal echocardiography (TEE), use of anesthetic agents, and bleeding and anticoagulation-related issues. The next two chapters will discuss issues related to CPB and myocardial protection.

I. Preoperative Visit

A. A preoperative visit by the cardiac anesthesiologist is essential before all operations. This provides an opportunity to review the patient's history, perform a relevant examination, and explain the techniques of monitoring and postoperative ventilatory support. This evaluation should identify any potential problems that might require further workup or could influence intraoperative management.

1. History: cardiac symptoms, significant comorbidities, previous anesthetic experiences, surgical procedures, allergies, medications, recent use of steroids

2. Examination: heart, lungs, intubation concerns (loose teeth, ability to open mouth, laxity of jaw)

B. The anesthesiologist should instruct the patient on which medications to continue up to the time of surgery and which ones to stop or have doses modified. Specifically, the anesthesiologist should tell the patient to:

1. Continue all antihypertensive and antianginal medications up to and including the morning of surgery. One exception may be the angiotensin-converting enzyme (ACE) inhibitors, which can be withheld to reduce the risk of low systemic resistance in the perioperative period.

2. Withhold the morning dose of insulin or oral hypoglycemic medications on the day of surgery. Blood sugars should be obtained on arrival in the operating room and frequently during surgery with coverage provided by intravenous insulin.

3. Confirm that the patient will be off anticoagulant and antiplatelet agents prior to elective surgery (clopidogrel for 1 week, aspirin for at least 3 days)[1,2] if possible, unless the surgeon has specified otherwise (check with the surgeon if not sure). For patients awaiting surgery in hospital, the anesthesiologist should communicate with the surgical team as to the timing of cessation of various anticoagulant

medications. These include unfractionated heparin, low-molecular-weight heparin (which should be stopped at least 12 hours preoperatively)[3], and IIb/IIIa inhibitors (which should be stopped at least 4 hours preoperatively).[4,5]

C. Obtain consent from the patient for the insertion of monitoring lines with a discussion of potential complications.

D. Order appropriate preoperative medications.

II. Preoperative Medications

These should be administered 30–60 minutes before the patient is brought to the operating room. They are given to reduce the patient's anxiety and produce amnesia to allow for the safe insertion of monitoring lines without producing hemodynamic stress. Commonly used medications include lorazepam 1–2 mg PO with morphine 0.1 mg/kg IM, often with scopolamine 0.2–0.4 mg IM in younger patients. Lighter doses of preoperative medications are usually required for patients with critical valve disease or markedly depressed ventricular function. Additional sedation with midazolam is commonly given during the insertion of central lines. Prophylactic antibiotics may be given on call to the operating room, but preferentially should be administered by the anesthesiologist at the time of line insertion to make sure that the antibiotic infusion has been completed by the time of skin incision.

III. Intraoperative Monitoring and Transesophageal Echocardiography

A. Patients undergoing cardiac surgical procedures are extensively monitored. Hemodynamic alterations and myocardial ischemia that occur during the induction of anesthesia, the prebypass period, during CPB, and following resumption of cardiac activity can have significant adverse effects on myocardial function and recovery. It should be noted that even though both hypertension and tachycardia can increase myocardial oxygen demand, an increase in heart rate (HR) results in more myocardial ischemia at an equivalent increase in oxygen demand.[6]

B. Standard monitoring equipment in the operating room consists of a five-lead ECG system, a noninvasive blood pressure cuff, a radial (and occasionally femoral) arterial line, a pulse oximeter, an end-tidal CO_2 measurement, a Swan-Ganz pulmonary artery catheter to monitor filling pressures and cardiac outputs and assess for ischemia,[7] and a urinary Foley catheter to measure urine output and core body temperature. In uncomplicated coronary artery bypass surgery patients with normal or mildly depressed ventricular function, use of a central venous pressure (CVP) monitoring line instead of a pulmonary artery catheter can provide an adequate assessment of filling pressures.[8,9] TEE has become fairly routine in most centers and is cost-effective in providing useful information.[10–14] There should be provisions to perform epiaortic scanning to assess for ascending aortic atherosclerosis.[15,16]

C. Swan-Ganz pulmonary artery catheters are usually placed before the induction of anesthesia, especially if left ventricular (LV) dysfunction is present. These catheters are used to measure right (CVP) and left-sided filling pressures (pulmonary artery diastolic [PAD] pressure or pulmonary capillary wedge [PCW] pressure) and obtain thermodilution cardiac outputs. Despite the nearly universal use of these catheters to carefully monitor patients and provide objective data on cardiac performance, studies have not conclusively demonstrated that they influence the outcome of cardiac surgery.[9,17–19]

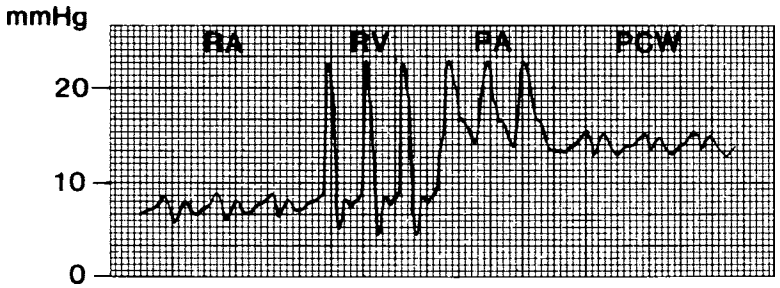

Figure 4.1 • Swan-Ganz catheter pressures. Intracardiac pressures are recorded from the distal (PA) port as the catheter is passed through the right atrium (RA), right ventricle (RV), and pulmonary artery (PA), into the pulmonary capillary wedge (PCW) position.

1. The catheter is usually inserted through an 8.5F introducer placed into the internal jugular vein or, less commonly, the subclavian vein.[20] The introducer sheath contains one side port that provides central venous access for the infusion of vasoactive medications and potassium. Multilumen introducers, such as the 8.5F and 9F high-flow advanced venous access (AVA) devices (Edwards Lifesciences and Arrow), can be used to provide additional venous access in patients with poor arm veins and limited peripheral access. A manifold with multiple stopcocks is attached to either the side port of the introducer or to one of the additional ports of the AVA through which all medications are administered.
2. The catheter is passed into the right atrium and the balloon at the catheter tip is inflated. The catheter is advanced through the right ventricle and pulmonary artery into the pulmonary capillary wedge position as confirmed by pressure tracings (Figure 4.1). The pulmonary artery tracing should reappear when the balloon is deflated. **Note:** Caution is essential when passing the catheter through the right ventricle in patients with a left bundle branch block in whom heart block might occur. In this situation, it is best to wait until the chest is open before advancing the catheter so that the surgeon can directly pace the heart if necessary.[21] External defibrillator or pacing patches may be useful.
3. The proximal port of the Swan-Ganz catheter (30 cm from the tip) is used for CVP measurements from the right atrium and for fluid injections to determine the cardiac output. Care must be exercised when injecting sterile fluid for cardiac outputs to prevent bolusing of vasoactive medications that might be running through the CVP port. **Note:** One must *never* infuse anything through this port if the catheter has been pulled back so that the tip lies in the right atrium and the CVP port lies outside the patient! This may not be noticed because the catheter is usually placed through a sterile sheath that allows for advancement or withdrawal of the catheter.
4. The distal port should always be transduced and displayed on a monitor to allow for detection of catheter advancement into the permanent wedge position, which could result in pulmonary artery injury. Balloon inflation ("wedging" of the catheter) is rarely necessary during surgery. Medications should never be given through the distal pulmonary artery port.

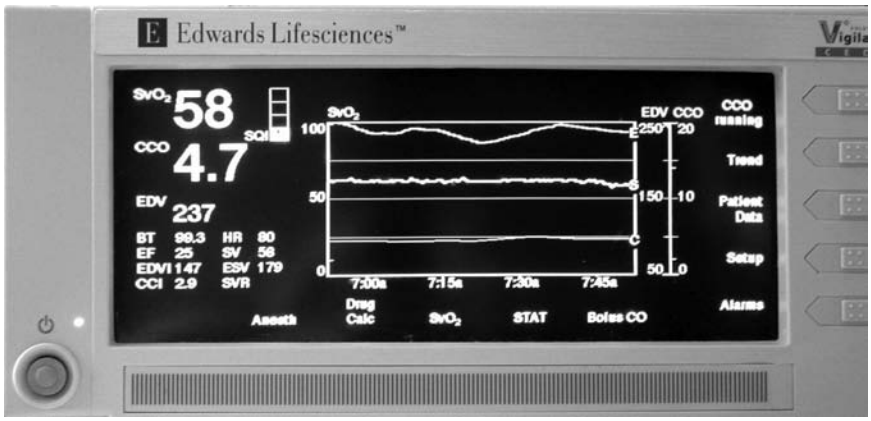

Figure 4.2 • Continuous cardiac output and mixed venous oxygen saturation obtained from a Swan-Ganz catheter commonly used during off-pump surgery. (*Image courtesy of Edwards Lifesciences, Inc.*)

5. A variety of Swan-Ganz catheters are available that provide additional functions.
   - **a.** Some catheters contain additional ports for volume infusion or for the placement of right atrial and ventricular pacing wires. The latter is helpful during minimally invasive surgery when access to the heart is limited.
   - **b.** Other catheters have been modified for assessment of continuous cardiac outputs and mixed venous O_2 saturations by fiberoptic oximetry (Figure 4.2). These catheters are invaluable during off-pump surgery to evaluate the patient's hemodynamic status and may contribute to a therapeutic maneuver in many patients.[22] Oximetric catheters are also helpful in patients with tricuspid regurgitation in whom thermodilution technology tends to underestimate the cardiac output.[23]
   - **c.** Volumetric Swan-Ganz catheters use thermodilution to determine the right ventricular (RV) end-diastolic and end-systolic volumes, allowing for calculation of an RV ejection fraction.[24] This is particularly valuable in patients with pulmonary hypertension and compromised RV function.
6. The primary concerns during insertion of a pulmonary artery catheter are arterial puncture, arrhythmias during passage through the right ventricle, and potential heart block in patients with preexisting bifascicular block. Other complications of Swan-Ganz catheters are noted in Chapter 7.
7. **Pulmonary artery perforation** is a very serious complication.[25–28] It may occur during insertion of the catheter or during the surgical procedure when hypothermia causes the catheter to become rigid. Since the cold, stiff catheter may advance into the lung when the heart is manipulated, it is advisable to pull it back during CPB and readvance it after CPB. Migration of the catheter into the wedge position may be evident by loss of pulse pressure in the pulmonary artery waveform before or after bypass or by a very high pulmonary arterial

pressure measurement on bypass when the heart is decompressed. The catheter should be pulled back a short distance to prevent perforation.

a. If perforation occurs, blood will appear in the endotracheal tube. The goals of management are to maintain gas exchange and then arrest the hemorrhage. Positive end-expiratory pressure (PEEP) should be applied to the ventilator circuit. If the degree of hemoptysis is not severe, it may abate once CPB is terminated and protamine is administered.

b. If the airway is compromised by bleeding, CPB should be resumed with venting of the pulmonary artery. Bronchoscopy is then performed with placement of a bronchial blocker or a double-lumen endotracheal tube that can provide differential lung ventilation. The pleural space should be entered to evaluate the problem. Occluding the hilar vessels and application of PEEP may resolve the bleeding, but if it is not controlled, pulmonary resection may be required. Use of femoral artery–femoral venous extracorporeal membrane oxygenation may control bleeding by lowering the pulmonary arterial pressures. Due to the risk of recurrence, pulmonary angiography and embolization may be considered once the bleeding is controlled.

D. Intraoperative TEE has become routine in most cardiac surgical centers.[10–14,29–33] The probe is placed after the patient is anesthetized and before heparinization. TEE provides an analysis of regional and global right and left ventricular function, is very sensitive in detecting the presence of ischemia,[34] and identifies the presence of valvular pathology (Table 4.1). Color flow Doppler is used to analyze valvular function or suspected shunts. Although TEE may image the aorta for atheromatous disease, epiaortic imaging provides better visualization of the ascending aorta and arch when there are significant concerns about atheromatous disease.[15,16] After

Table 4.1 • Specific Uses of Intraoperative Echocardiography

All patients	Epiaortic imaging for aortic atherosclerosis Evaluation of cardiac performance (regional/global dysfunction) Evaluation of iatrogenic aortic dissections
Coronary disease	Regional dysfunction (incomplete/inadequate revascularization)
Valve surgery	Prebypass identification of valvular pathology Valve regurgitation from paravalvular leak or inadequate repair Outflow tract obstruction after mitral valve repair Valve obstruction Residual stenosis after commissurotomy Presence of intracardiac air
IABP	Location of device relative to the aortic arch
VSD closure	Residual VSD

bypass, TEE can be used to assess ventricular function, the presence of intracardiac air,[35] and the efficacy of valve repairs and replacements. An individual trained in performing and reading TEE, whether a cardiac anesthesiologist or a cardiologist, is essential to optimize its usefulness. Before the probe is placed, consideration must be given to contraindications to TEE that could produce catastrophic complications, such as esophageal perforation. These include previous esophageal surgery,

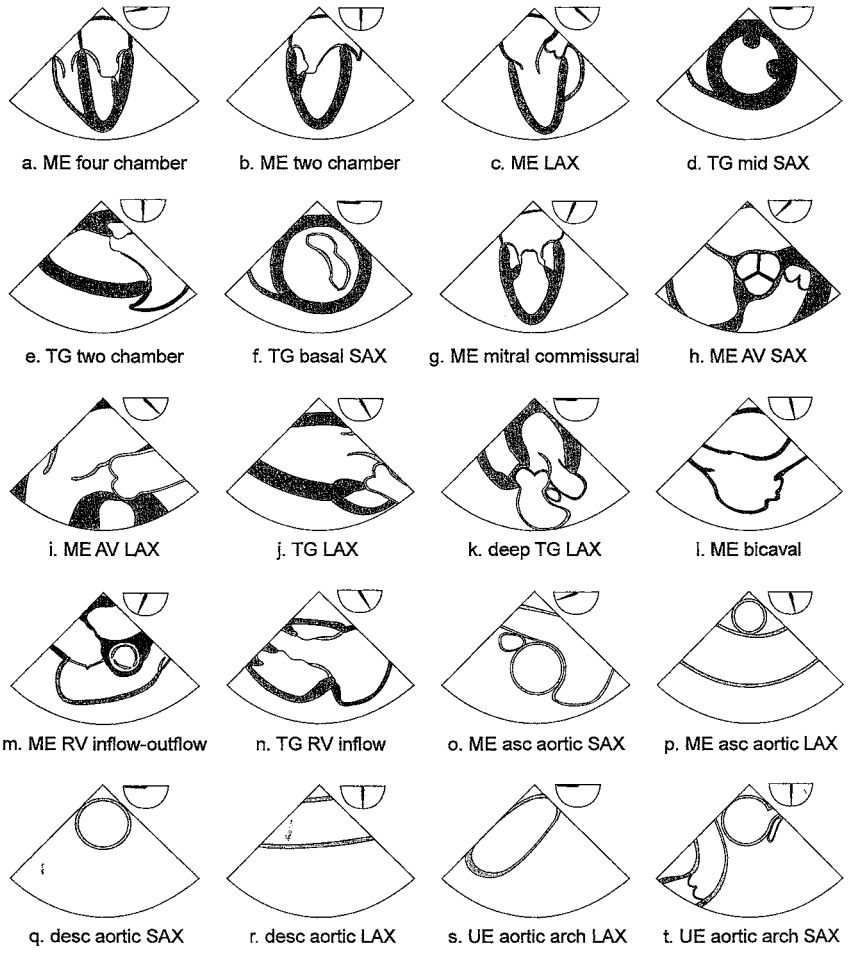

Figure 4.3 • Recommended views for intraoperative transesophageal echocardiography. *(Reproduced with permission from Shanewise JS, Cheung AT, Aronson S, et al. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: Recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for certification in perioperative transesophageal echocardiography. Anesth Analg 1999;89:870–84.)*

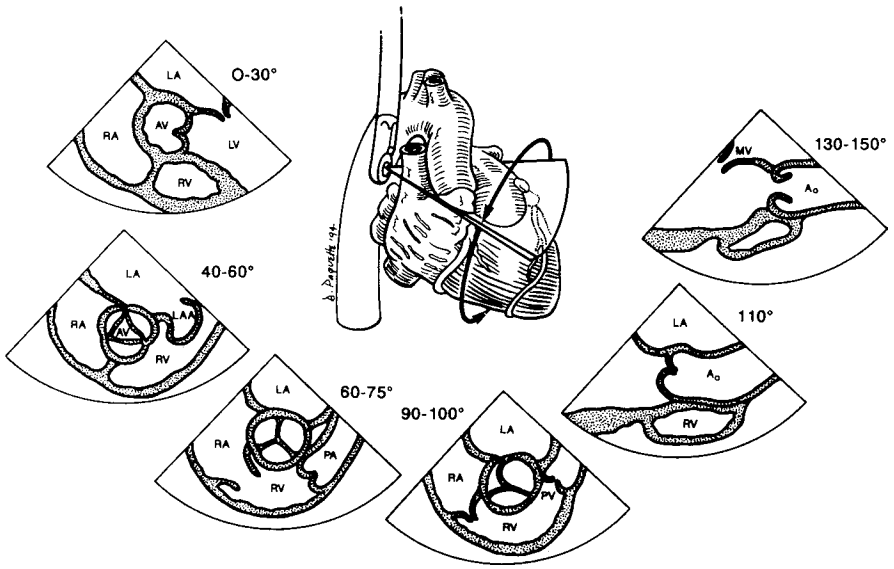

Figure 4.4 • Upper-midesophageal echocardiographic imaging of the aortic valve. Rotation of the probe allows for visualization of the aortic valve and proximal ascending aorta in short- and long-axis views. *(Reproduced with permission from Roelandt J, Pandian NG, eds. Multiplane Transesophageal Echocardiography. New York: Churchill Livingstone, 1996:33–58.)*

and known esophageal pathology, such as strictures, Schatzki's ring, or esophageal varices.[36,37]

1. Multiplane TEE has become standard and allows for rotation of the probe through 180 degrees, thus affording excellent images of the heart in multiple views. The probe is advanced up and down the esophagus and then into the stomach for transgastric views. The tip of the probe can be flexed in four different directions, and the shaft of the probe can also be rotated. The American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists have defined 20 standard views for a routine examination (Figure 4.3).[31] Some of the best views during cardiac surgery include the following.
2. In the mid-upper esophagus, rotation of the probe allows for visualization of the aortic valve and proximal ascending aorta in short- and long-axis views (Figure 4.4).
3. In the mid-lower esophagus, the standard views can be obtained by rotating the probe through 135 degrees. With progressive rotation, these views include a four-chamber view (0 degrees), long-axis two-chamber view (90 degrees), and a long-axis view of the LV outflow tract (130–150 degrees) (Figure 4.5).
4. With the probe anteflexed in the transgastric views, the three standard views are the short axis of the right ventricle and left ventricle (0 degrees), longitudinal two-chamber LV view (70–90 degrees), and the LV outflow tract (110–135 degrees) (Figure 4.6).[29–31]

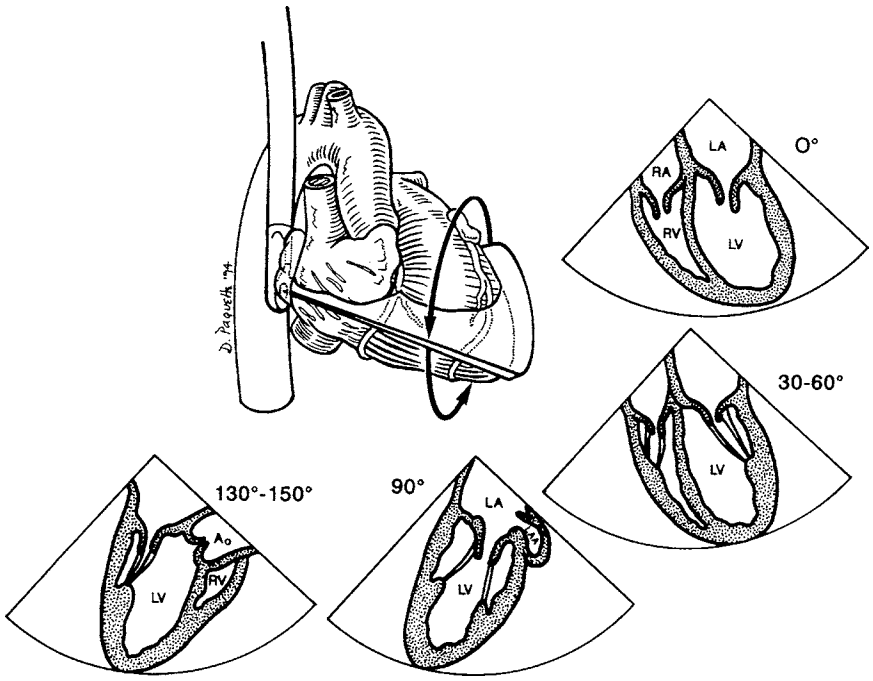

Figure 4.5 • Mid-lower esophageal echocardiographic imaging. Standard views can be obtained by rotating the probe through 135 degrees. With progressive rotation, these views include a four-chamber view (0 degrees), long-axis two-chamber view (90 degrees), and long-axis view of the LV outflow tract (130–150 degrees). *(Reproduced with permission from Roelandt J, Pandian NG, eds. Multiplane Transesophageal Echocardiography. New York: Churchill Livingstone, 1996:33–58.)*

5. During on-pump coronary artery surgery, prebypass TEE will provide a baseline analysis of regional and global ventricular function. The midpapillary long- and short-axis views are best to assess most regions of the left ventricle. The ability of the heart muscle to thicken is consistent with viability, whereas areas of thinned-out muscle represent infarcted areas. Following bypass, slight improvement in previously ischemic zones may be noted, especially with inotropic stimulation. These areas of hypokinesis may represent stunned or hibernating myocardium that have contractile reserve and may gradually recover function after revascularization. The new onset of hypokinesis raises the specter of hypoperfusion from an anastomotic or graft problem, incomplete revascularization, or inadequate myocardial protection. The new onset of mitral regurgitation (MR) may reflect loading conditions but could indicate ischemia.
6. During off-pump surgery, the midesophageal windows are best for assessing RV and LV function and the presence of MR. Baseline views are obtained. During vessel occlusion, TEE should assess for the acute development of regional LV dysfunction or acute MR during construction of left-sided grafts and for RV dysfunction during right coronary grafting. The transgastric views

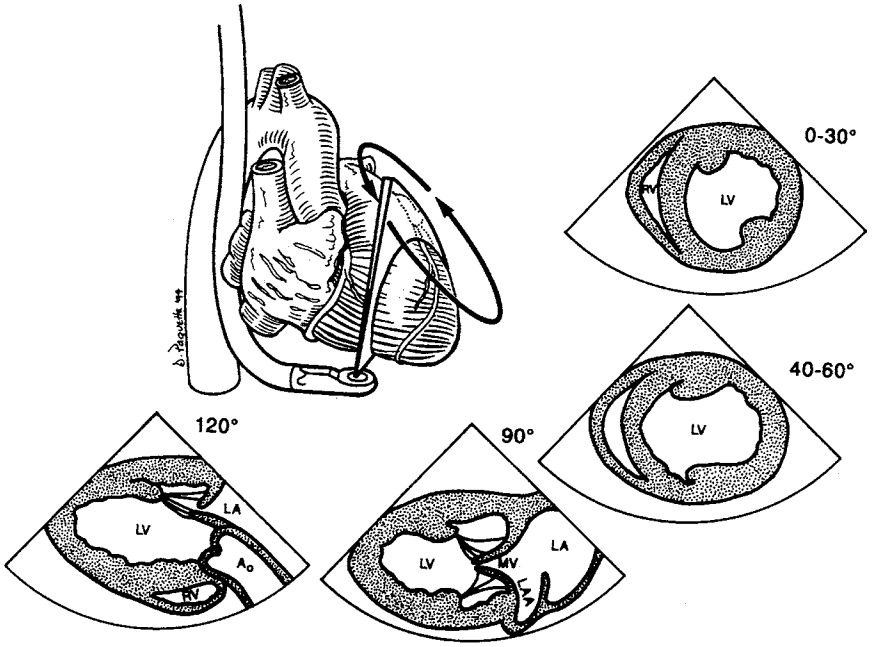

Figure 4.6 • Transgastric views. With the probe anteflexed in the transgastric views, the standard views are the short axis of the right ventricle and left ventricle (0 degrees), longitudinal two-chamber LV view (90 degrees), and the LV outflow tract (120 degrees). *(Reproduced with permission from Roelandt J, Pandian NG, eds. Multiplane Transesophageal Echocardiography. New York: Churchill Livingstone, 1996:33–58.)*

are not helpful when the heart is elevated out of the chest.[33] The development and persistence of a new regional wall motion abnormality after a graft is completed suggests a flow problem, usually at the anastomosis. However, the latter may occur even in the absence of a regional wall motion abnormality.

7. In minimally invasive procedures (usually aortic or mitral valve surgery), TEE can confirm the location of the retrograde coronary sinus catheter since it cannot be palpated by the surgeon.
8. In aortic valve operations, the best views are obtained from the mid- to upper esophagus (see Figure 4.4). TEE can quantify the degree of aortic stenosis by planimetry and pressure gradients, quantify the degree of aortic regurgitation by color flow analysis that can influence delivery of cardioplegia, and assess the degree of LV hypertrophy and its nature (concentric, septal). Annular size can be assessed. The presence of severe diastolic rather than systolic dysfunction may influence pharmacologic management. After bypass, valve opening and closing can be assessed and paravalvular leaks may be identified. Competence of homografts and autografts (Ross procedure) can be confirmed. Rarely, an unusual finding may be demonstrated, such as an aorto–left atrial fistula or ventricular septal defect (VSD).

9. The best visualization of the mitral valve is from the lower and middle esophagus. Prebypass assessment should confirm the valvular pathology and identify the mechanism of MR (e.g., a flail leaflet and the direction of the regurgitant jet). However, in some patients with MR, it is not uncommon to note a discrepancy between preoperative and intraoperative TEE due to alteration in loading conditions. Left atrial clot should be sought. During weaning from bypass, TEE is helpful in identifying intracardiac air.[35] After termination of bypass it should be used to assess the competence of valve repairs, identify paravalvular leaks after valve replacement, and assess LV and RV function. Occasionally, the TEE will reveal an unsuspected finding, such as systolic anterior motion of the anterior mitral valve leaflet obstructing the LV outflow tract, evidence of valve dysfunction with a trapped or obstructed leaflet, or aortic insufficiency after a difficult mitral valve operation (due to suture entrapment of an aortic valve cusp or distortion of the aortic annulus from placement of too small a mitral valve).

10. The diagnosis of an aortic dissection can be confirmed by TEE once the patient is anesthetized. It not only identifies the intimal flap, but can also determine whether aortic insufficiency is present, mandating aortic valve resuspension or replacement. If a large pericardial effusion is present, groin cannulation may be necessary for the emergency institution of CPB before opening the pericardium. TEE can also identify flaps in cases of iatrogenic dissections at cannulation or clamp sites.

11. In thoracic aortic surgery, TEE is useful in assessing cardiac performance and intracardiac volume status during the period of clamping and after unclamping, when pulmonary arterial pressures tend to be elevated out of proportion to preload. This may influence fluid and pharmacologic management.[38]

IV. Anesthetic Considerations for Various Types of Heart Surgery

A. Anesthetic management must be individualized, taking into consideration the patient's age, comorbidities, the nature and extent of coronary or valvular disease, and the degree of LV dysfunction. These factors will determine which medications should be selected to avoid myocardial depression, tachycardia, or bradycardia, or counteract changes in vasomotor tone. Generally, narcotic-based anesthesia is used for all open-heart surgery to minimize myocardial depression. Specific anesthetic concerns for various disease processes are presented in this section.

B. Coronary bypass surgery

1. Factors that increase myocardial oxygen demand, such as tachycardia and hypertension, must be prevented in the prebypass period, especially during the induction of anesthesia. Hypotension, often resulting from the use of narcotics and anxiolytics, such as midazolam, should be counteracted with fluids and α-agents since hypotension is more likely to produce ischemia than hypertension.

2. Detection and treatment of ischemia is critical in the prebypass period. TEE is the most sensitive means of detecting ischemic regional wall motion abnormalities but is not always used in "routine" cases.[34] Ischemia may also be manifested by an elevation in the pulmonary arterial pressures or by ST-segment elevation in the ECG leads. Aggressive management with nitroglycerin, β-blockers

(esmolol), and narcotics can usually control prebypass ischemia. If not, prompt institution of CPB may be necessary.

3. Narcotic/sedative regimens are the standard for coronary surgery, especially in patients with LV dysfunction. Use of low-dose fentanyl or sufentanil, inhalational anesthetics, midazolam, and propofol allows for early postoperative extubation.
4. Anesthetic techniques for **off-pump surgery** commonly involve use of a continuous cardiac output Swan-Ganz catheter with on-line mixed venous oxygen saturation monitoring. Tilting of the operating room table (Trendelenburg position and to the right) to augment cardiac filling, judicious fluid administration, antiarrhythmic therapy (lidocaine/magnesium), α-agents (phenylephrine) and inotropes (epinephrine/milrinone), and, on occasion, insertion of an intraaortic balloon pump (IABP) may be used. The essential elements to a successful off-pump operation include a patient surgeon who uses good judgment in deciding when off-pump surgery is feasible and when conversion to CPB or right-heart assist is necessary, an anesthesiologist who is experienced and comfortable with off-pump surgery, and a qualified, actively involved first assistant (see section IX on page 163 for a more detailed discussion of anesthesia for off-pump surgery).

C. Left ventricular aneurysms. Anesthetic drugs that cause myocardial depression must be avoided because of the association of LV aneurysms with significant LV dysfunction. Swan-Ganz monitoring is important in optimizing preload and contractility before and after bypass. TEE is the most sensitive means of detecting the presence of LV thrombus.

D. Ventricular septal defects are usually operated upon on an emergent basis when the patient is in cardiogenic shock, usually on inotropic support and often with an IABP. Thus, myocardial depression must be avoided. Systemic hypertension may increase the shunt and should be prevented.

E. Aortic stenosis. The induction of anesthesia is a critical period for patients with aortic stenosis. Narcotic-based anesthesia is used to minimize hemodynamic alterations such as myocardial depression, vasodilation, tachycardia, or dysrhythmias, all of which can lower cardiac output precipitously. An α-agent, such as phenylephrine or norepinephrine, is particularly valuable in supporting systemic resistance. The best TEE views of the aortic valve are obtained in the midesophageal short- and long-axis views.

F. Aortic insufficiency. The hemodynamic goals in the prebypass period are to maintain satisfactory preload and avoid bradycardia and hypertension. Vasodilation may be beneficial, but hypotension may reduce the diastolic perfusion pressure and precipitate ischemia. The transgastric long-axis view with color Doppler is best for assessing aortic insufficiency.

G. Hypertrophic obstructive cardiomyopathy. Measures that produce hypovolemia or vasodilatation must be avoided because they increase the outflow tract gradient. Volume infusions should be used to maintain preload with the use of α-agents to maintain systemic resistance. Use of β-blockers and calcium channel blockers to reduce heart rate and contractility are beneficial in the immediate preoperative and prebypass periods. Inotropic drugs with predominantly β-adrenergic effects should be avoided.

H. Mitral stenosis. Attention should be paid to maintaining preload, reducing heart rate, and preventing an increase in pulmonary vascular resistance (PVR).

1. Preload must be adjusted judiciously to ensure adequate LV filling across the stenotic valve while simultaneously avoiding excessive fluid administration that could lead to pulmonary edema. A volumetric (RV ejection fraction) Swan-Ganz catheter is valuable in the assessment of RV volumes and ejection fractions. The PA diastolic pressure may overestimate the left atrial pressure and may require placement of a left atrial line for monitoring after bypass. Balloon inflation (wedging) of a pulmonary artery catheter should be avoided or performed with a minimal amount of balloon inflation in patients with pulmonary hypertension because of the increased risk of pulmonary artery rupture.
2. The heart rate should be reduced to prolong the diastolic filling period. For patients in atrial fibrillation (AF), small doses of esmolol can be used to control a rapid ventricular response. Atropine should be avoided as a premedication. Nonetheless, cardiac output is usually marginal in patients with mitral stenosis and can be further compromised if the ventricular rate is excessively slow.
3. Factors that can increase PVR must be avoided. Preoperative sedation should be light to prevent hypercarbia. Hypoxemia, hypercarbia, acidosis, and nitrous (not nitric) oxide should be avoided in the operating room. The PVR can be reduced with pulmonary vasodilators before bypass (usually nitroglycerin), and with inotropic agents after bypass that can produce pulmonary vasodilatation (inamrinone, milrinone, or isoproterenol). Nesiritide, prostaglandin E_1 (PGE_1), nitric oxide, or Iloprost can be used to reduce PVR if there is evidence of severe RV failure (see pages 254 and 356).

I. Mitral insufficiency

1. Measures that can increase pulmonary arterial pressure, such as hypoxemia, hypercarbia, acidosis, and nitrous oxide, should be avoided. Preoperative sedation should be light.
2. In the prebypass period, adequate preload must be maintained to ensure forward output. Systemic hypertension should be avoided because it tends to increase the amount of regurgitation. If the patient has ischemic MR or a borderline cardiac output, use of systemic vasodilators or intraaortic balloon pumping will improve forward flow.
3. TEE is invaluable in identifying the precise anatomic cause for MR and in evaluating the surgical result. This is performed once the patient is anesthetized. Occasionally, there is a discrepancy between preoperative and intraoperative studies due to alterations in systemic resistance and loading conditions. Elevating the blood pressure with α-agents may increase the amount of regurgitation in patients with moderate ischemic MR and aid in the decision to repair the valve during bypass surgery. Midesophageal and transgastric long-axis views with rotation of the probe can evaluate the mitral valve quite precisely.

J. Tricuspid valve disease

1. Maintenance of an elevated CVP is essential to achieve satisfactory forward flow. A Swan-Ganz pulmonary artery catheter can be placed for monitoring of left-sided pressures in patients with tricuspid regurgitation, although cardiac

output determinations are of little value. A Swan-Ganz catheter can be used after valve repair or tissue valve replacement, but not after mechanical valve replacement. Alternatively, a left atrial line and pulmonary artery thermistor can be placed for cardiac output determinations. Other means of assessing cardiac output (esophageal Doppler or bioimpedance) can also be used.

2. A normal sinus mechanism provides better hemodynamics than AF, although the latter is frequently present. Slower HRs are preferable for tricuspid stenosis and faster HRs for tricuspid regurgitation.
3. Measures that avoid myocardial depression and lower the PVR may be helpful in improving RV function.
4. In patients with hepatic congestion, a coagulopathy may develop after CPB. Aprotinin should be considered in these patients and fresh frozen plasma should be available due to depletion of coagulation factors normally produced by the liver.

K. Endocarditis

1. Anesthetic management is dictated by the hemodynamic derangements associated with the particular valve involved.
2. Patients with aortic valve endocarditis may have evidence of heart block from involvement of the conduction system by periannular infection. This may require preoperative placement of a transvenous pacing wire.
3. Ongoing sepsis may produce refractory hypotension on pump despite use of α-agents. Vasopressin may be necessary to maintain the blood pressure.

L. Aortic dissections

1. Maintenance of hemodynamic stability and especially avoidance of hypertension are critical to prevent aortic rupture, especially during the induction of anesthesia and line insertion. Use of a Swan-Ganz catheter is important to optimize perioperative hemodynamics. Its insertion can be delayed until after intubation to minimize the stress response.
2. Most patients require emergency surgery and should be considered to have a full stomach. A modified rapid sequence induction should be performed to minimize the risk of aspiration while ensuring hemodynamic stability.
3. TEE is invaluable in localizing the site and often the extent of the dissection, the degree of aortic insufficiency, and the presence of hemopericardium. This must be performed **very cautiously** in the awake patient with a suspected dissection for fear of precipitating hypertension, rupture, and then tamponade. If the diagnosis has been confirmed by other means, TEE should be performed in the anesthetized patient.
4. Repair of type A dissections is usually performed during a period of deep hypothermic circulatory arrest. The head is packed in ice, and medications are given to potentially provide additional cerebral protection (see section M.1).
5. Repair of type B dissections requires a period of descending aortic cross-clamping. Because less collateral flow is present in patients with dissections than with atherosclerotic aneurysms, the risk of paraplegia is greater. A cerebrospinal fluid (CSF) drainage catheter should be placed before the patient is anesthetized. Proximal hypertension must be controlled during application of the cross-clamp but should not be so low as to compromise spinal cord perfusion.

M. Ascending aortic and arch aneurysms

1. Aneurysms limited to the proximal and mid-ascending aorta are repaired with CPB and application of an aortic cross-clamp. If they extend more distally or the arch is extensively involved, a period of deep hypothermic circulatory arrest at 18°C is used. This should provide 45–60 minutes of safe arrest time in minimizing the risk of neurologic insult. Adjuncts to improve cerebral protection include packing the head in ice, and administration of methylprednisolone 30 mg/kg and thiopental or pentobarbital 5–10 mg/kg. Continuous retrograde perfusion of the superior vena cava (SVC) may be used to maintain cerebral hypothermia, and the CVP should be monitored and kept less than 20 mm Hg. Alternatively, antegrade perfusion of the cerebral vessels may be provided.
2. Profound hypothermia and warming are associated with a coagulopathy. Platelets, fresh frozen plasma, and cryoprecipitate are helpful in achieving hemostasis. Supplemental use of warming devices, such as the Arctic Sun device (MediVance, Inc., Louisville, CO), is helpful in warming the patient faster and preventing temperature afterdrop.
3. Aprotinin is arguably helpful in reducing intraoperative bleeding with use of deep hypothermic circulatory arrest, although there are concerns about adverse neurologic sequelae.[39] Proponents of aprotinin believe that it is safe as long as certain measures are taken. This includes ensuring an adequate activated clotting time (kaolin ACT > 750–1000 seconds), giving additional heparin (1 mg/kg just prior to period of circulatory arrest), and stopping the infusion of aprotinin during the arrest period.[40–42] Alternatively, aprotinin may be given just during the rewarming phase.

N. Descending aortic aneurysms

1. Arterial monitoring lines are inserted in the right radial and the right femoral artery to monitor proximal and distal pressures during the period of aortic cross-clamping. The femoral line is valuable when left-heart bypass techniques are used.
2. A Swan-Ganz catheter is important to monitor filling pressures during the period of cross-clamping. TEE is helpful in evaluating myocardial function and often demonstrates a hypovolemic LV chamber despite elevated pulmonary arterial pressures when the cross-clamp is removed.[38] Ensuring adequate intravascular volume will reduce the risk of "declamping shock" upon release of the aortic cross-clamp.
3. One-lung anesthesia using a double-lumen or Univent tube improves operative exposure.
4. Several medications have been used in an attempt to improve renal perfusion during the period of aortic cross-clamping. An infusion of fenoldopam 0.03–0.1 μg/kg/min appears to be promising.[43]
5. Control of proximal hypertension is essential during the cross-clamp period. A catheter for CSF drainage should be placed before the patient is positioned and anesthetized to reduce the incidence of spinal ischemia. Nitroprusside must be used cautiously because it can reduce renal and spinal cord perfusion and increase CSF pressure.[44]

O. Implantable cardioverter-defibrillator placement

1. ICD implantation is usually performed in an electrophysiology laboratory under moderate sedation with midazolam, allowing the patient to breath spontaneously.

When ventricular fibrillation is induced, deepening of the level of sedation with propofol and assisted ventilation usually suffice. This requires close nursing or anesthesia attendance and careful monitoring. Most patients have markedly depressed ventricular function. Provisions for cardiac resuscitation (personnel and equipment) should be immediately available. External defibrillator pads should be placed for rescue defibrillation.

2. Medications that could be potentially arrhythmogenic, such as the catecholamines, must be avoided. Antiarrhythmic medications are continued unless there are plans for an electrophysiologic study, which is usually performed with the patient off medications.

P. Surgery for atrial fibrillation

1. Procedures to correct AF may not be successful for several months. Therefore, medications used for rate control or for AF prophylaxis can be continued up to the time of surgery.
2. Other considerations pertain to the specific lesion for which surgery is being performed if the arrhythmia surgery is an adjunctive procedure.

Q. Surgery for pericardial disease

1. Cardiac output and blood pressure are dependent on adequate preload, increased heart rate, and increased sympathetic tone. Swan-Ganz monitoring is helpful in maintaining adequate preload and in assessing the hemodynamic response to the procedure. Agents that produce vasodilatation, bradycardia, or myocardial depression must be avoided. Volume infusions and α-agents are beneficial in maintaining hemodynamic stability. Since loss of sympathetic tone can be catastrophic in a patient with tamponade physiology, prepping and draping of the patient before the induction of anesthesia should be strongly considered.
2. TEE is invaluable in identifying the size and hemodynamic effects of an effusion. With limited surgical approaches, such as a subxiphoid window or thoracoscopy, it can identify whether the effusion has been adequately drained.
3. After resolution of tamponade, filling pressures generally fall, blood pressure increases, and a brisk diuresis occurs. Depending on the duration of tamponade, some patients may require transient inotropic support after the fluid is removed.
4. After the constricted heart is decorticated, filling pressures may transiently fall, but many patients develop a low output state associated with ventricular dilatation requiring inotropic support. Inadequate decortication may be evident when a fluid challenge that restores the preoperative filling pressures fails to increase cardiac output. Pulmonary edema may develop if the surgeon decorticates the right ventricle while the left ventricle remains constricted.

V. Induction and Maintenance of Anesthesia

A. Cardiac anesthesia is provided by a combination of medications that includes induction agents, anxiolytics, amnestics, analgesics, muscle relaxants, and inhalational anesthetics.

B. Induction agents include thiopental, propofol, etomidate, ketamine, and the benzodiazepines. Most commonly, anesthesia is induced with a combination of thiopental, narcotics, and neuromuscular blockers to provide muscle relaxation and prevent chest wall rigidity that is associated with high-dose narcotic inductions. Ketamine given

Table 4.2 • Hemodynamic Effects of Commonly Used Anesthetic Agents

Agent	HR	Contractility	SVR	Net Effect on BP
Induction Agents				
Thiopental	↑	↓	↓	↓
Propofol	↓	↓	↓↓	↓↓
Etomidate	↔	↔	↔	↔
Anxiolytics				
Midazolam	↑	↔	↓	↓
Propofol	↓	↓	↓↓	↓↓
Lorazepam	↔	↔	↓	↓
Narcotics				
Fentanyl	↓	↔	↓	↓
Sufentanil	↓↓	↔	↓	↓
Alfentanil	↓	↔	↓	↓
Remifentanil	↓	↔	↓	↓
Muscle Relaxants				
Pancuronium	↑	↔	↔	↑
Vecuronium	↔	↔	↔	↔
Doxacurium	↔	↔	↔	↔
Atracurium	↔	↔	↓	↓
Rocuronium	↔	↔	↔	↔
Succinylcholine	↑↓	↓	↔	↑↓

with a benzodiazepine is very useful in patients with compromised hemodynamics or tamponade. Ketamine does not produce myocardial depression, and its dissociative effects and sympathetic stimulant properties that produce hypertension and tachycardia are attenuated by use of a benzodiazepine.[45]

C. Subsequently, anesthesia is maintained by additional dosing of narcotics and muscle relaxants in combination with an anxiolytic (midazolam or propofol) and an inhalational agent (Tables 4.2 and 4.3). Bispectral (BIS) electroencephalographic monitoring can be used to titrate and minimize the amount of medication required to maintain adequate anesthesia (a level around 55–60) while preventing awareness.[46,47] This is useful during bypass when hemodilution increases the effective volume of distribution and may necessitate redosing of anesthetic medications. The dose and selection of anesthetic agents must provide adequate anesthesia and analgesia during surgery, but may be modified to allow for extubation in the operating room or, more commonly, several hours after arrival in the ICU.

Table 4.3 • Dosages and Metabolism of Commonly Used Anesthetic Agents

Agent	Usual Dosage	Duration of Action
Induction Agents		
Thiopental	3–5 mg/kg	5–10 min
Propofol	1–3 mg/kg → 10–100 μg/kg/min	2–8 min
Etomidate	0.2–0.4 mg/kg → 5–10 μg/kg/min	3–8 min
Anxiolytics		
Propofol	25–75 μg/kg/min	Up to 20 min
Midazolam	2.5–5 mg IV q2h or 1–4 mg/h	Up to 10 h
Lorazepam	1–4 mg q4h or 0.02–0.05 mg/kg	4–6 h
Narcotics		
Fentanyl	5–10 μg/kg → 1–5 μg/kg/h	1–4 h
Sufentanil	0.5–1 μg/kg → 0.25–0.75 μg/kg/h	1–4 h
Alfentanil	50–75 μg/kg → 0.5–3 μg/kg/min	1–1.6 h
Remifentanil	1 μg/kg → 0.05–2 μg/kg/min	10 min
Muscle Relaxants		
Pancuronium	0.1 mg/kg → 0.01 mg/kg q1h	180–240 min[a]/0–60 min[b]
Vecuronium	0.1 mg/kg → 0.01 mg/kg q30–45 min	45–90 min[a]/25–40 min[b]
Doxacurium	0.06 mg/kg → 0.005 mg/kg q30 min	180–240 min[a]/45–60 min[b]
Atracurium	0.4–0.5 mg/kg → 0.3–0.6 mg/kg/h	30–45 min[a]/15–30 min[b]
Rocuronium	0.6–1.2 mg/kg IV	30–60 min
Succinylcholine	1 mg/kg	5–10 min

[a]After initial intubating dose.
[b]After repeat dose.

D. Traditional regimens that included high-dose fentanyl have been supplanted by protocols using low-dose fentanyl, sufentanil, or alfentanil.[48–50] The least expensive regimen combines low-dose fentanyl with an inhalational anesthetic to facilitate early extubation. Sufentanil has a half-life of about 20–40 minutes and allows patients to awaken within hours of completion of the operation. Remifentanil is a very short-acting narcotic with a context-sensitive half-life of 3–5 minutes that may be beneficial in shorter operations and in elderly patients.[51–54] Although more expensive, it allows for a reduction in the dose of propofol and is usually selected for patients who can be extubated promptly after surgery. Thus, it has not been shown to increase overall hospital costs.[54]

E. Midazolam has been shown to have an elimination half-life of more than 10 hours in patients undergoing cardiac surgery.[55] Although early extubation can be achieved in patients receiving midazolam throughout surgery, most groups limit its use to the prebypass period and then initiate a propofol infusion at the termination of bypass and continue it in the ICU. Propofol can be used to control post-bypass hypertension because of its strong vasodilator properties. When the patient is stable, the propofol is turned off and the patient is allowed to awaken.[56]

F. Inhalational agents provide muscle relaxation and unconsciousness, with variable effects on myocardial depression.[57] Agents commonly used include isoflurane, enflurane, desflurane, and sevoflurane. They are generally given during CPB to maintain anesthesia and reduce blood pressure, and allow for usage of lower doses of intravenous medications, although they provide no analgesia. Desflurane and sevoflurane have less lipid solubility with a rapid onset of action and are quickly reversible, allowing for early extubation. Nitrous oxide is contraindicated in that it reduces the amount of oxygen that can be delivered and may also increase pulmonary arterial pressures.

G. Muscle relaxants are given throughout the operation to minimize patient movement and suppress shivering during hypothermia. Adequate muscle relaxation might reduce some of the paraspinal muscle soreness often noted after surgery due to sternal retraction.

1. Pancuronium is the most commonly used neuromuscular blocker. It increases both heart rate and blood pressure and mitigates narcotic-induced bradycardia and hypotension. In contrast, vecuronium and doxacurium have very few hemodynamic effects. Rocuronium is a short-acting neuromuscular blocker with a rapid onset of action and vagolytic properties. It is especially helpful for the induction of anesthesia. Atracurium does not undergo renal elimination and is the best agent to use in patients with renal insufficiency (see Tables 4.2 and 4.3).[58–60]

2. Although some centers reverse muscle relaxants at the end of the operation, this can be detrimental if the patient becomes agitated and develops hemodynamic alterations. A conservative approach is to observe the patient in the ICU for several hours during which time most of the neuromuscular blockade dissipates and extubation can then be achieved. **Adequate sedation must be maintained in the ICU while a patient remains pharmacologically paralyzed**.

H. Dexmedetomidine is an α_2-adrenergic agonist with numerous properties, including sedation, analgesia, anxiolysis, and sympatholysis. During surgery, it can be used to reduce the dosage of other medications, allowing for early, comfortable extubation. It may also reduce shivering and myocardial ischemia.[61,62] Its role in perioperative management is still being defined.[63] It is given as a loading dose of 1 μg/kg over 10 minutes followed by a continuous infusion of 0.2–0.7 mg/kg/h.

VI. Prebypass Considerations

A. Avoidance of ischemia prior to initiating bypass is critical for all types of heart surgery. Identification of ischemic electrocardiographic changes, elevation in filling pressures, or regional wall motion abnormalities on TEE requires prompt attention. Manipulation of the heart by the surgeon for cannula placement, blood loss during redo dissections, ongoing blood loss from leg incisions, and AF during atrial cannulation are a few of the potential insults that must be addressed. Judicious use of fluids and α-agents to counteract vasodilatation and hypotension, β-blockers or additional anesthetic agents for hypertension or tachycardia, and nitroglycerin for ischemia must be selected appropriately to maintain stable hemodynamics. In the prebypass period, fluids are usually administered in the form of crystalloid.

B. **TEE** should be performed at this time to provide a baseline assessment of regional wall motion abnormalities and identify known or overlooked valvular pathology.[29–32]

C. **Autologous blood withdrawal** before the institution of bypass protects platelets from the damaging effects of CPB. The quality of this blood is excellent, with only slight activation of platelets, and it has been demonstrated to preserve red cell mass and reduce transfusion requirements.[64] It should be considered in patients for whom the calculated hematocrit on pump will remain adequate after withdrawal of 1–2 units of blood with nonheme fluid replacement.

D. Pharmacologic intervention may be considered to reduce the systemic inflammatory response to bypass. This may include use of aprotinin (see below) or steroids. Although use of preoperative methylprednisolone or dexamethasone may reduce the inflammatory response, little clinical benefit other than an improvement in emetic symptoms or appetite has been demonstrated.[65–68]

E. **Antifibrinolytic drugs** have been demonstrated unequivocally to reduce perioperative blood loss in cardiac operations. They should be used for all on-pump cardiac surgical procedures and may be of benefit in off-pump cases as well.[69–72] Most protocols include giving the first dose at the time of skin incision or before heparinization, giving a dose in the pump prime, and administering a constant infusion during the operation (Box 4.1).

1. **Aprotinin** is a serine protease inhibitor that has been demonstrated in numerous studies to be extremely effective in reducing perioperative bleeding and also in producing an antiinflammatory effect.[73]

a. Mechanisms of action of aprotinin include:

i. Preservation of platelet function by blocking the platelet glycoprotein Ib receptor.

ii. Inhibition of fibrinolysis by inhibiting circulating plasmin directly and by blocking kallikrein-induced conversion of plasminogen to plasmin.

iii. Inhibition of kallikrein-induced kinin formation, minimizing its vasoactive effects that contribute to increased vascular permeability.

iv. Inhibition of neutrophil activation and degranulation.

v. Decrease in complement activation.

b. Because aprotinin is so effective in reducing perioperative bleeding, there have been concerns about its prothrombotic tendencies, especially in patients with small coronary arteries.[74] However, it has been shown that aprotinin selectively blocks the proteolytically activated thrombin receptor (PAR1) on platelets, thus inhibiting platelet aggregation induced by thrombin

Box 4.1 • Doses of Antifibrinolytic Drugs

Aprotinin	(1) High dose:	2 million KIU prior to heparinization 2 million KIU in pump prime 0.5 million KIU/h
	(2) Low dose:	half of above
	(3) Weight adjusted:	3.5 mg/kg IV bolus 70 mg pump prime load 3.5 mg/kg/h for 1 hour 1 mg/kg/h continuous infusion[83]
ε-aminocaproic acid	5 g prior to heparinization 5 g in pump prime 1 g/h during surgery	
Tranexamic acid	(1) 10 mg/kg over 20 minutes followed by a 1 mg/kg/h infusion[99,103] (2) 1-g bolus followed by an infusion of 400 mg/h with 500 mg in the pump prime[93] (3) 100 mg/kg given before CPB[104] (4) 5.4 mg/kg load, 50 mg in the pump prime (for a 2.5-L circuit), and a 5 mg/kg/h continuous infusion[98]	

(antithrombotic effect). At the same time, it does not inhibit platelet aggregation induced by collagen or adenosine diphosphate (ADP), thus allowing for normal hemostatic activity in surgical wounds.[75] Most studies have not demonstrated adverse effects of aprotinin on graft patency.[76] Additionally, use of high-dose, but not low-dose, aprotinin reduces the risk of stroke.[77]

c. Because of its expense, aprotinin should generally be reserved for complex operations, reoperations, and other situations where the bleeding risk is increased (hepatic dysfunction, thrombocytopenia, uremia, use of aspirin and possibly clopidogrel).[78,79]

d. Traditionally, aprotinin protocols have been subdivided into high-dose, low-dose, and ultra-low-dose as follows:

i. High-dose aprotinin: 2 million kallikrein inactivation units (KIU) (280 mg) after the induction of anesthesia over 30 minutes, 2 million KIU (280 mg) in the pump prime, and a maintenance infusion of 0.5 million KIU/h (70 mg/h) until the completion of the operation.

ii. Half-dose aprotinin: 1 million KIU (140 mg) after induction, 1 million KIU (140 mg) in the pump prime, and a continuous infusion of 250,000 KIU/h (35 mg/h).

iii. "Minimal dose" and "ultra-low-dose" protocols include giving 0.5 million KIU (70 mg) before incision with additional 0.5 million KIU (70 mg) on pump or giving 1–2 million KIU (140–280 mg) in the pump prime alone.

e. The antifibrinolytic effects of aprotinin are noted at plasma concentrations of 125 KIU/L, which is sufficient to inhibit 90% of plasmin activity. This may be seen with lower dosing regimens and is effective in reducing bleeding. However, the antiinflammatory effects require a plasma level of 200 KIU/mL, which is required to inhibit kallikrein by approximately 50%.[80–82] This usually requires the higher dosing regimen.

f. Due to the expense of using aprotinin, weight-based protocols to maintain a serum level of 200 KIU/mL have been devised.[83,84] The recommendation of the Mayo clinic group is as follows:
   i. 3.5 mg/kg IV bolus
   ii. 70-mg pump prime load
   iii. 3.5 mg/kg/h for 1 hour, then 1 mg/kg/h continuous infusion

g. Aprotinin is useful in minimizing uremic bleeding due to platelet dysfunction in patients with dialysis-dependent renal failure. However, in patients with moderate renal dysfunction, it must be used cautiously because it may worsen renal function. Approximately 20% of patients will develop an increase in serum creatinine >0.5 mg/dL and 4% will have more than a 2 mg/dL increase, both of which are greater than in patients not receiving aprotinin.[85] Aprotinin is actively absorbed by the renal tubular system where it remains for 5–6 days and produces reversible overload of tubular reabsorption mechanisms. Patients with normal preoperative renal function usually compensate for this abnormality with little increase in creatinine, but those with altered tubular function may sustain additional tubular injury. Although guidelines for dosing in patients with moderate renal dysfunction are not available, lower doses should probably be used because of the increased half-life in patients with renal dysfunction.[86–88] Note that aprotinin is removed by intraoperative hemofiltration; this must be taken into consideration when hemofiltration is used during surgery to remove fluid.

h. Aprotinin raises the ACT and can lead to underheparinization. Aprotinin is absorbed by kaolin, so a kaolin ACT >480 seconds is adequate. It is not absorbed by celite, so a celite ACT must exceed 750 seconds.[89] If readily available, heparin levels should be measured and maintained >2.7 IU/mL.

i. There has been a reported association of neurologic deficits and renal dysfunction in patients undergoing deep hypothermic circulatory arrest with the use of aprotinin.[39] Safe use of aprotinin involves administering additional heparin before the period of circulatory arrest to achieve a higher ACT (at least >600 seconds and perhaps >1000 seconds), maintaining a heparin level >2.7 U/kg, recirculating the pump during the period of circulatory arrest, and avoiding infusion of aprotinin during the arrest period. Alternatively, the aprotinin infusion can be initiated during the rewarming phase.

j. Despite its antigenic properties (50% of patients will have detectable IgG immunoglobulins within 3 months of exposure), allergic reactions upon reexposure to aprotinin are relatively uncommon (about 3%).[90] Nonetheless, reexposure is best avoided for 6 months. A small test dose of 1 mL is optional before an initial dose of aprotinin because a severe anaphylactic reaction has been reported upon primary exposure.[91]

2. ε-aminocaproic acid (Amicar) is an inexpensive medication that can be used to reduce blood loss in first-time and uncomplicated reoperations. It has antifibrinolytic properties and may also preserve platelet function by inhibiting the

conversion of plasminogen to plasmin. It has no effect on the ACT. Although a meta-analysis concluded that it was as effective as aprotinin in reducing bleeding after cardiac surgery,[92] many studies have not demonstrated this, consistent with most surgeons' experiences.[93]

- **a.** One common regimen is to give 5 g after the induction of anesthesia, 5 g on pump, and 1 g/h during the procedure. Twice this dose is commonly used in patients weighing more than 100 kg. Giving a 5–10-g dose only at the time of heparinization for bypass also reduces blood loss.
- **b.** A pharmacokinetic study showed that the clearance of ε-aminocaproic acid decreases and the volume of distribution increases during CPB. To maintain a plasma level of 260 μg/mL, a recommended dosing regimen of a 50 mg/kg load over 20 minutes followed by a maintenance infusion of 25 mg/kg/h has been recommended.[94]
- **c.** Few adverse clinical effects have been noted with use of ε-aminocaproic acid. There is no increased risk of stroke.[95] Although a subtle degree of renal tubular dysfunction may occur, as demonstrated by an increase in urine β_2-microglobulin levels, a 10 g dose was not shown to alter creatinine clearance.[96,97]
- **d.** ε-Aminocaproic acid is primarily effective when given prophylactically, but might be of benefit in reducing blood loss if given only after bypass by inhibiting fibrinolysis. If extensive bleeding is encountered after its prophylactic use, aprotinin may be considered to control bleeding. However, the combination of these two medications might theoretically promote a prothrombotic state, and this must be taken into consideration if one takes this approach.

3. **Tranexamic acid** (Cyclokapron) has similar properties to ε-aminocaproic acid, inhibiting fibrinolysis at a serum concentration of 10 μg/mL, and reducing plasmin-induced platelet activation at a level of 16 μg/mL.[98] It has been shown to reduce perioperative blood loss in on- and off-pump surgery[71,99] and in several studies was found to be as effective as aprotinin.[100,101] It does not affect the ACT.[102]
   - **a.** The appropriate dosing of tranexamic acid is not well defined. One common recommendation is 10 mg/kg over 20 minutes followed by a 1 mg/kg/h infusion; another is a 1 g bolus followed by an infusion of 400 mg/h with 500 mg in the pump prime. [93,99–101,103] Another study showed that one dose of 100 mg/kg given before CPB was very effective in reducing bleeding.[104]
   - **b.** A weight-based protocol to achieve a plasma level >20 μg/mL entails a 5.4 mg/kg load, 50 mg in the pump prime (for a 2.5-L circuit), and a 5 mg/kg/h continuous infusion, to be modified by the serum creatinine.[98]
   - **c.** Topical use of tranexamic acid in the pericardial space has been shown to significantly reduce perioperative bleeding.[105]
   - **d.** Tranexamic acid is substantially less expensive than aprotinin, but more expensive than ε-aminocaproic acid.

F. Anticoagulation for cardiopulmonary bypass

1. Anticoagulation is essential during CPB to prevent the production of thrombin and fibrin monomers caused by interaction of blood with a synthetic interface. Advances in the design of extracorporeal circuits, such as heparin-bonded systems (Carmeda, Duraflo), have reduced, but not completely eliminated, the necessity for anticoagulation (see Chapter 5).[106,107]

2. **Heparin dosing.** Heparin inhibits the coagulation system by binding to antithrombin III. It also contributes to platelet dysfunction and induces a fibrinolytic state.[108,109] A baseline ACT should be drawn after the operation has commenced and before systemic heparinization. A small dose of heparin (5000 units) is given before division of the internal thoracic artery or radial artery, but a total dose of approximately 3–4 mg/kg of heparin must be given prior to cannulation for CPB. Porcine heparin may be associated with a lower risk of heparin antibody formation than bovine heparin and is therefore preferentially recommended.[110]
3. **Heparin** monitoring is performed using a number of systems that measure the ACT. This widely used test qualitatively assesses the anticoagulant effect of heparin. Although a standard dose of heparin is usually given, there is great variability in patient response to heparin. An individualized dose-response curve that relates the heparin dose to its effect on the ACT can be performed to determine the requisite amount of heparin. The ACT is influenced by many factors besides heparin, including hypothermia, hemodilution, and, to a lesser degree, thrombocytopenia. Furthermore, the ACT does not measure or necessarily correlate with heparin concentrations. Achieving higher patient-specific heparin levels more effectively suppresses hemostatic system activation than standard dosing based on ACT alone.[111] Nonetheless, due to its simplicity and overall safety, achieving a satisfactory ACT level is acceptable and universally utilized. The ACT should be monitored every 20–30 minutes during bypass (or prior to bypass if there is a significant delay after initial heparinization) and additional heparin administered as necessary.
   a. The ACT should be maintained over 480 seconds throughout the pump run. Lower ACTs are acceptable with the use of heparin-coated circuits during routine coronary bypass surgery, but probably are not acceptable during complex open heart operations.[106,107]
   b. With the use of aprotinin, which itself raises the ACT level, kaolin ACTs must be maintained longer than 480 seconds, whereas celite ACTs must exceed 750 seconds to avoid underheparinization.
   c. During off-pump surgery, the optimal ACT is not known. Using 2.5 mg/kg of heparin with a target ACT over 300 seconds is satisfactory and is not associated with any increased risk of thrombotic complications.[112]
   d. Because of individual patient variability in response to heparin and the effects of hypothermia and hemodilution on the ACT, anticoagulation can also be assessed by calculating dose-response curves and measuring circulating levels of heparin (desired level is >2.7 U/mL) using the Medtronic Hepcon system. This directly measures circulating heparin levels and also allows for determination of a neutralizing dose of protamine to return the ACT to baseline.[113]
   e. An alternative means of assessing anticoagulation is the high-dose thrombin time. This correlates better with heparin concentration and is not affected by temperature, hemodilution, or aprotinin.[114]
4. **Heparin resistance** is present when a heparin dose of 5 mg/kg fails to raise the ACT to an adequate level (>400 seconds). This is an unpredictable occurrence but is more commonly noted in patients on preoperative heparin, IV nitroglycerin, an IABP, and in patients with infective endocarditis.[115] It is usually related to antithrombin III deficiency. If additional heparin does not elevate the ACT,

antithrombin III must be given, either in fresh frozen plasma or in a commercially available pooled product (Thrombate III), which provides 500 units per vial.[116–118]

5. **Heparin-induced thrombocytopenia** documented by positive serologic tests (enzyme-linked immunosorbent assay) or platelet aggregation testing (heparin-platelet factor 4 or serotonin release assay) poses a dilemma for the patient requiring cardiac surgery.[119] Ideally, surgery should be delayed for about 3 months, at which time antibodies have usually disappeared. At that time, a heparin challenge is considered to be safe and is usually not associated with the reappearance of antibodies. However, when surgery is necessary on a more urgent basis and HIT is confirmed (i.e., *both* antibodies and thrombocytopenia are present), the readministration of heparin can produce profound thrombocytopenia and widespread thrombosis. Not infrequently, a heparin antibody is present in patients receiving preoperative heparin (up to 35% in one study),[120] but in the absence of thrombocytopenia its presence is not a contraindication to use of heparin during surgery. However, when HIT is present, an alternative means of achieving satisfactory anticoagulation during CPB and for off-pump surgery must be employed. Several regimens have been investigated (Table 4.4).
   a. Standard doses of heparin can be used in association with the three following options:
      i. Preoperative **aspirin and dipyridamole** as platelet pretreatment (a somewhat risky approach).[121]
      ii. Platelet inhibition with the short-acting **glycoprotein IIb/IIIa inhibitors** (tirofiban or eptifibatide). One recommended dosing regimen for tirofiban is 10 μg/kg 10 minutes prior to administration of standard-dose heparin, followed by a continuous infusion of 0.15 μg/kg/min that should be stopped 1 hour before the anticipated cessation of CPB. The effects of tirofiban on platelet function cannot be reversed, but 80% of their effect dissipates within 4 hours. Thus, bleeding may persist for a period of time after CPB has terminated.[122]
      iii. **Prostaglandin analogs** (PGE_1, epoprostenol [prostacyclin], or iloprost) can be used to inhibit platelet function during heparinization.
         - PGE_1 is given in a dose of 0.5–1.0 μg/min.
         - Epoprostenol is given in a dose of 5 ng/kg/min and increased by 5 ng/kg increments every 5 minutes (to observe for systemic hypotension) up to 25–30 ng/kg/min, following which a heparin bolus is given. After protamine administration, the dose is weaned in 5 ng/kg decrements.[123]
         - Iloprost can be given starting at a dose of 3 ng/kg/min with a doubling of dose every 5 minutes to a dose determined by preoperative in vitro testing. The usual dose required is 6–24 ng/kg/min.[124]
   b. **Bivalirudin** is a synthetic hirudin analog that is a direct thrombin inhibitor. It has a rapid onset of action and a half-life of 25 minutes. It is primarily metabolized by proteolytic cleavage by thrombin in the bloodstream. There is some renal elimination, so modification is necessary in patients with renal dysfunction. The effects of bivalirudin cannot be reversed, but it can be eliminated by hemofiltration and plasmapheresis.[125] After discontinuation, it is not associated with a hypercoagulable state (cf. argatroban).

Table 4.4 • Alternative Drugs for Anticoagulation During Cardiopulmonary Bypass in Patients with Heparin-Induced Thrombocytopenia

Drug	Half-life	Reversal	Metabolism	Monitoring	Dosing Regimen
Bivalirudin	25 min	None	Metabolic > renal	ACT, ECT	1.5 mg/kg bolus, 50 mg in pump, then 2.5 mg/kg/h infusion
Lepirudin	80 min	None	Renal	PTT, ECT	0.25 mg/kg, 2 mg/kg in pump prime, 0.5 mg mg/min infusion
Argatroban	30 min	None	Hepatic > renal	PTT, ACT	0.1 μg/kg bolus, then 5–10 μg/kg/min
Danaparoid	20 h	None	Renal	Factor Xa levels	125 U/kg, 3 U/kg in pump prime, 7 U/kg/h

i. For off-pump surgery, bivalirudin has been given as a loading dose of 0.75 mg/kg followed by an infusion of 1.75 mg/kg/h to obtain an ACT of 300–350 seconds.[126]

ii. For on-pump surgery, the recommended dose is a 1.5 mg/kg initial bolus, followed by a continuous infusion of 2.5 mg/kg/h infusion with 50 mg placed in the pump.[119] The infusion rate is then modified depending on the ecarin clotting time (ECT) as noted below. Other studies have used a 50-mg bolus followed by an infusion of 1.5–1.75 mg/kg/h.[127,128]

iii. Adequacy of anticoagulation can be monitored with an ACT or an ECT drawn every 30 minutes. Studies have suggested that plasma bivalirudin levels of 10–15 μg/mL should be achieved. The correlation of the ECT with plasma levels is as follows: >500 seconds (> 15 μg/mL), 400–500 seconds (10–15 μg/mL), and <400 seconds (<10 μg/mL).[119,129]

c. **R-hirudin** (lepirudin) is a recombinant hirudin analog that is a direct thrombin inhibitor. It has a slow onset of action and a long half-life, estimated at around 80 minutes in a patient with normal renal function. Since it is primarily excreted by the kidneys, any impairment in renal function contraindicates its use. Its effects cannot be reversed, although it can be eliminated by hemofiltration.[130] Significant bleeding has been reported in most cases in which lepirudin has been used.

i. The recommended dosing regimen is 0.25 mg/kg before CPB, 0.2 mg/kg in pump prime, and a continuous infusion of 0.5 mg/min. It should be discontinued 15–30 minutes before the anticipated end of CPB.[131,132]

ii. The ACT is unreliable in assessing anticoagulation with hirudin at levels required for CPB. Thus, anticoagulation must be monitored by the ECT, attempting to achieve a level of 400–450 seconds. This corresponds to a hirudin level greater than 4 μg/mL.[119]

d. **Argatroban** is a direct thrombin inhibitor that takes about 1–3 hours to reach a steady-state level and has a half-life of about 30 minutes. It is primarily metabolized by the liver with about 25% excretion by the kidneys. Thus it is preferable to lepirudin in patients with renal impairment. It is monitored by the ACT, aiming for a level of 300–400 seconds. For off-pump surgery, one recommended dose is 2.5 μg/kg/min to achieve an ACT of twice baseline.[133] For on-pump surgery, the recommended dose is 0.1 mg/kg followed by a continuous infusion of 5–10 μg/kg/min.[134]

e. **Danaparoid** sodium is a heparinoid that inhibits factor Xa, resulting in inhibition of thrombin generation. It has low cross-reactivity with antiheparin antibodies (about 10%). Although it has been used during cardiac surgery, its disadvantages are that it has a half-life of 20 hours, undergoes renal metabolism, and its effects are not reversible.[135,136] Thus, it is invariably associated with significant bleeding after CPB.

i. The recommended dosing protocol is 125 antifactor Xa U/kg IV bolus, 3 U/kg in the pump prime, and a continuous infusion of 7 U/kg/h that should be stopped 45 minutes before the anticipated end of CPB.

ii. Appropriate monitoring requires measurement of factor Xa levels, trying to maintain a plasma concentration of 0.7–1.3 U/mL. Since such testing is not feasible during CPB, this medication is very risky and has been associated with thrombotic events on bypass. Although useful in postoperative patients with HIT, it is best avoided during CPB. It is no longer available in the United States.

G. Although one dose of antibiotics administered prior to skin incision usually suffices to provide adequate tissue levels, an additional 1-g dose of cefazolin may be beneficial just before going on bypass.

VII. Considerations During Cardiopulmonary Bypass

A. Virtually all valve surgery and most coronary bypass surgery is performed using CPB. The essential components of the CPB circuit are discussed in the next chapter. Basically, the blood drains by gravity from the right atrium into a reservoir, is oxygenated, cooled or warmed, and then returned to the patient through an arterial cannula usually placed in the ascending aorta. Desired hemodynamic and laboratory values during bypass are noted in Table 5.2.

B. The lungs are not ventilated during bypass since oxygenation occurs within the oxygenator and carbon dioxide is eliminated by the gas flow into the oxygenator (the sweep rate). Although studies have suggested that the efficacy of gas exchange postpump is improved in patients whose lungs remain inflated during CPB, this is not a common practice.[137] Arterial blood gases are measured to ensure that the oxygenator is providing adequate oxygenation and that CO_2 extraction is sufficient. Venous oxygen saturation is measured to determine if the systemic flow rate is adequate. If on-line monitoring is not available, studies should be repeated every 15–20 minutes.

C. The optimal mean blood pressure during CPB is controversial.[138,139] Although there is some evidence that a higher mean blood pressure (around 80 mm Hg) may reduce some of the neurocognitive changes seen after bypass, the standard management is to maintain a mean blood pressure around 65 mm Hg using vasodilators (narcotics or inhalational anesthetics) or vasopressors (phenylephrine, norepinephrine, or vasopressin). Perfusion pressure is determined by a number of variables.

1. Hypotension may be related to hemodilution; use of preoperative vasodilators, including ACE inhibitors, calcium channel blockers, and amiodarone; vasodilatation during rewarming; and autonomic dysfunction. It may also occur due to inadequate systemic flow rates, impairment of venous drainage, aortic insufficiency, administration of cardioplegia, and during return of large amounts of cardiotomy-suctioned blood into the circulation.
2. Hypertension may be related to vasoconstriction, the level of anesthesia and analgesia, elevation in endogenous catecholamine levels, and alterations in acid-base balance and blood gas exchange.

D. A venous oxygen saturation exceeding 65% indicates that the systemic flow rate is satisfactory, although there may be differences in regional flow (i.e., less to the kidneys and splanchnic circulation). It tends to be higher during systemic hypothermia due to lessened oxygen extraction, and may decrease significantly during rewarming, necessitating an increased flow rate.

E. Studies have suggested that cerebral blood flow is more dependent on blood pressure than on flow rate.[140,141] If flow rate is adequate, α-agents must be utilized to maintain a blood pressure of at least 40 mm Hg and probably higher. Cerebral blood flow is maintained by autoregulation until the pressure falls below 40 mm Hg, but this response is inadequate in diabetic and hypertensive patients, in whom a higher pressure must be maintained. Measurement of cerebral oxygenation by cerebral oximetry using bifrontal sensors with near-infrared spectroscopy

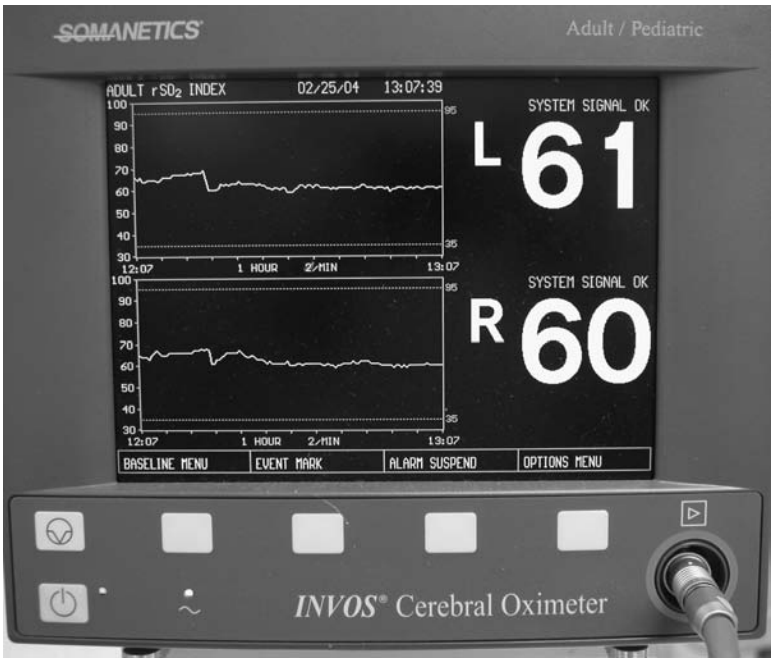

Figure 4.1 • The Somanetics INVOS Cerebral Oximeter. This device uses near infrared spectroscopy to measure the regional oxygen saturation of predominantly venous blood directly in the brain through optical sensors placed on the right and left side of the forehead. *(Image courtesy of Somanetics Corporation)*

(Somanetics INVOS Cerebral Oximeter) can be used to assess the adequacy of cerebral perfusion (ScO_2) during on-pump and off-pump surgery (Figure 4.7)[142–144] There is increasing evidence that modifications in anesthetic and perfusion management by changes in flow rate, blood pressure, PCO_2, and/or hematocrit in response to a fall in ScO_2 below 40 mm Hg reduces neurological complications.[145]

F. Blood sugar tends to be elevated due to the hormonal stress response to surgery and CPB with insulin resistance. The infusion of insulin to control blood sugar has not been shown to reduce inotropic requirements or the occurrence of arrhythmias but may reduce the incidence of neurocognitive dysfunction.[146,147]

G. Measures to optimize renal function should be considered in patients with preoperative renal dysfunction (creatinine >1.5 mg/dL), especially in diabetic, hypertensive patients. The primary considerations should be maintaining a higher mean perfusion pressure (around 80 mm Hg) and keeping the pump run as short as possible (or avoiding it entirely with off-pump techniques). Pharmacologic means to optimize renal perfusion may include fenoldopam (0.03–0.1 μg/kg/min) or nesiritide, although the potential renoprotective role of nesiritide has not yet been defined.[148–150] Although both renal-dose dopamine (3 μg/kg/min) and furosemide may increase urine output during CPB, neither has been found to be renoprotective.[151–153] In fact, furosemide has been shown to increase the incidence of postoperative renal dysfunction.[151] However, the major cause of postoperative renal dysfunction is a low

output state, so maintenance of satisfactory hemodynamics at the termination of CPB is essential so that any intraoperative renal insults are transient.

H. When the cross-clamp is removed, lidocaine and magnesium may be given to reduce the incidence of atrial and ventricular arrhythmias.[154] Ventricular fibrillation tends to occur when the heart was maintained at a cold temperature during the period of cardioplegic arrest and usually requires defibrillation, although spontaneous conversion to a sinus mechanism may occur.

VIII. Termination of Bypass and Reversal of Anticoagulation

A. Once the cardiac portion of the operation has been completed, the lungs are ventilated and pacing is initiated, if necessary. Just prior to weaning bypass, 1 g of calcium chloride may be given to increase systemic vascular resistance (SVR) and provide some initial inotropic support.

B. Inotropic medications can be started prior to terminating bypass if it is anticipated that the heart may require some support. This should be considered in patients with preexisting LV dysfunction, prebypass ischemia, recent infarction, suboptimal or incomplete revascularization, LV hypertrophy, and long cross-clamp periods. If α-agents (phenylephrine, norepinephrine) were necessary on pump to support systemic pressure, they are usually necessary for a brief period of time after CPB is terminated.

C. Bypass is weaned by gradually reducing the venous return, increasing intravascular volume in the patient, and reducing the arterial flow rate.

D. **Arterial blood pressure** monitoring is often inconsistent due to the presence of peripheral vasoconstriction. Measurement of the central aortic pressure using a stopcock on the aortic line is very helpful in sorting out discrepancies. If this problem persists for more than 10–15 minutes, it is helpful to insert a femoral arterial monitoring line.[155,156]

E. TEE is utilized as the patient is being weaned from bypass to (see Table 4.1):

1. Identify intracardiac air. This is essential in valvular heart procedures or any procedure in which the left side of the heart has been entered (including venting). It is particularly valuable during minimally invasive procedures in which exposure to the heart for deairing is limited.

2. Assess regional and global ventricular function and loading conditions. TEE is the only means of assessing intravascular volume directly (other than by direct visualization) since the volume-pressure relationship is altered by decreased ventricular compliance. Thus, it is helpful in determining whether hypotension should be treated by volume infusions, inotropic medications, or α-agents.

3. Detect paravalvular leaks or the competence of a valve repair

F. If hemodynamic performance is not ideal, the anesthesiologist must work in concert with the surgeon in assessing myocardial function and the need for inotropes.[157] When myocardial performance is adequate, fluid administration to optimize preload is sufficient to obtain adequate hemodynamics. Initially this can be achieved by transfusing volume from the pump. After protamine administration, the blood remaining in the pump is processed through the cell-saving device and returned to the patient. If this is not immediately available, a colloid is often chosen to maintain intravascular volume. Albumin is preferable to hetastarch, which has been shown to increase bleeding and transfusion requirements.[158]

1. Once the patient is off bypass, visual inspection of the heart, assessment of serial cardiac outputs and filling pressures with a Swan-Ganz catheter, and TEE can be used to assess ventricular function and identify potential problems. For example, a new regional wall motion abnormality may suggest a technical problem with graft flow that can be remedied. If intracardiac air is identified, it is not uncommon for it to pass into the right coronary artery, causing RV dysfunction and dilatation. An additional short course on bypass with deairing of the aorta and any bypass grafts usually suffices. This is not an uncommon phenomenon in mitral valve surgery.
2. Fluid loading with concomitant TEE assessment and cardiac output measurements is helpful is determining the optimal filling pressures for subsequent management, although it is anticipated that filling pressures will eventually fall with improvement in cardiac performance. It should be remembered that the heart is less compliant after a period of ischemic arrest, and higher filling pressures will be necessary to achieve adequate intravascular volume.
3. If necessary, inotropic support is usually initiated with a catecholamine, such as epinephrine (1–2 μg/min) or dobutamine (5–10 μg/kg/min). If cardiac performance remains unsatisfactory, use of either inamrinone or milrinone is extremely helpful in unloading the heart and providing inotropic support. Their preemptive use just prior to terminating bypass has been suggested as a means of ameliorating postoperative deterioration in cardiac performance and oxygen transport, and reducing the need for catecholamine support.[159]
4. If cardiac performance is still suboptimal, reinstitution of CPB to reperfuse the heart at a low workload will frequently result in improved ventricular function. If the heart still does not function well, insertion of an IABP is usually necessary. When all of the above fail, consideration must be given to use of a circulatory assist device.

G. Protamine is a polycationic peptide administered to counteract the effects of heparin and is usually given in a 1:1 mg/mg ratio to return the ACT to baseline. Despite complete neutralization of heparin, the ACT may remain elevated in patients with significant thrombocytopenia or coagulopathies. Although moderate thrombocytopenia has not been shown to increase the ACT in patients with normally functioning platelets, it does seem to increase it when associated with platelet dysfunction after bypass.160 Thus, although additional protamine can be administered for a slightly elevated ACT, it will not necessarily return the ACT to baseline.
   1. The Medtronic Hepcon system provides a heparin-protamine titration test that can be utilized to measure heparin levels in the bloodstream and determine the appropriate dose of protamine necessary to neutralize the remaining heparin. Use of this system usually results in less protamine being administered than empiric dosing based on the heparin dose. Thus it can avoid the unnecessary use of protamine to correct an abnormal ACT that is not attributable to excessive heparin. Use of lower doses of protamine has been shown to restore platelet responsiveness to thrombin and attenuate platelet α-granule secretion.[161]
   2. Residual heparin effect may account for an elevated ACT. Thus it is not inappropriate to give small additional doses of protamine to try to reduce the ACT

to baseline. Infusion of blood that is spun down in the cell-saving devices does contain some heparin (up to 10% of the heparin is retained), and additional protamine (about 50 mg) may be useful to counteract its effects.

3. "Heparin rebound" may occur when heparin reappears in the bloodstream after protamine neutralization. This is more likely to occur in patients who have received large doses of heparin during bypass and is more common in obese patients.[162] This may occur because the half-life of protamine is only about 5 minutes.[163] An elevated ACT or PTT commonly reflects this phenomenon and can be reversed with additional doses of protamine.
4. Empiric use of large amounts of additional protamine should be discouraged because protamine itself is an anticoagulant and may contribute to mediastinal bleeding. Although a dose exceeding that of heparin by 3:1 is usually necessary to produce this effect, studies have demonstrated that an elevated PT from protamine can occur when the ratio exceeds 1.5:1.[164]
5. Hemodynamic studies have shown that intravenous administration of protamine may cause histamine release from the lungs, contributing to a decrease in systemic resistance and blood pressure, an effect not seen with intraarterial injection.[165] Nonetheless, other studies have shown no hemodynamic benefit to intraarterial as opposed to intravenous administration of protamine.[166]

H. Protamine reactions are unusual and are often unpredictable, although they have been noted with greater frequency in patients taking NPH insulin (risk may be increased 30- to 50-fold), those with fish or medication allergies, those with previous protamine exposure, and those who have had vasectomies.[167–169] Awareness of the possibility of their development and a prompt response if a reaction is noted are essential because protamine reactions are associated with increased perioperative mortality.[170,171]

1. **Type I.** Systemic hypotension from rapid administration (entire neutralizing dose after CPB given within 3 minutes). This is caused by a histamine-related reduction in systemic and pulmonary vascular resistance. It can be avoided by infusing the protamine over a 10–15 minute period and should be reversible with α-agent support.
2. **Type II.** Anaphylactic or anaphylactoid reaction resulting in hypotension, tachycardia, bronchospasm, flushing, and pulmonary edema.
   a. IIA. Idiosyncratic IgE- or IgG-mediated anaphylactic reaction. Release of histamine, leukotrienes, and kinins produces a systemic capillary leak causing hypotension and pulmonary edema. This tends to occur within the first 10 minutes of administration.
   b. IIB. Immediate nonimmunologic anaphylactoid reaction.
   c. IIC. Delayed reactions, usually occurring 20 minutes or more after the protamine infusion has been started, probably related to complement activation and leukotriene release, producing wheezing, hypovolemia, and noncardiogenic pulmonary edema from a pulmonary capillary leak.
3. **Type III.** Catastrophic pulmonary vasoconstriction manifested by elevated pulmonary arterial pressures, systemic hypotension from peripheral vasodilatation, decreased left atrial pressures, RV dilatation, and myocardial depression. This reaction tends to occur about 10–20 minutes after the protamine infusion has started. One proposed mechanism involves activation of complement

by the heparin-protamine complex that triggers leukocyte aggregation and release of liposomal enzymes that damage pulmonary tissue leading to pulmonary edema. Activation of the arachidonic acid pathway produces thromboxane, which constricts the pulmonary vessels. Pulmonary vasoconstriction usually abates after about 10 minutes.

4. Prevention of protamine reactions is usually not possible. Skin testing has not proved of any value. In patients considered at high risk, type II reactions might be attenuated by the prophylactic use of histamine blockers (cimetidine 300 mg IV, diphenhydramine 50 mg IV) and steroids (hydrocortisone 100 mg IV). This common practice has not been shown clinically to be of much benefit.
5. Treatment of protamine reactions involves correction of hemodynamic abnormalities that are identified. They must be differentiated from other conditions that can cause hemodynamic deterioration, such as hypoperfusion, air embolism, poor myocardial protection, or valve dysfunction. Measures must be taken to support systemic blood pressure while reversing pulmonary vasoconstriction if it is also present. Preparations to reinstitute CPB are frequently necessary. The following options may be effective:
   a. Calcium chloride 500 mg IV to support systemic resistance and provide some inotropic support.
   b. α-agents (phenylephrine, norepinephrine) to support systemic resistance.
   c. β-agents for inotropic support that can also reduce pulmonary resistance (low-dose epinephrine, dobutamine, inamrinone, milrinone).
   d. Drugs to reduce preload and pulmonary pressures (nitroglycerin, PGE_1, nitric oxide).[172]
   e. Aminophylline for wheezing.
   f. Readministration of heparin has been used to reverse the protamine reaction.[173,174]

I. **Alternatives to reverse anticoagulation.** Although simply not reversing heparin and administering clotting factors may suffice in ameliorating the bleeding tendency of heparinization,[175] other measures have been evaluated to arrest bleeding without use of protamine.
   1. **Heparinase-I** is a heparin-degrading enzyme that reverses the ACT in a dose-dependent fashion without causing hemodynamic changes. It is given as a bolus injection of 7–10 mg/kg. Although it returns the ACT to normal, it neutralizes only 70% of antifactor Xa (protamine neutralizes 100%) and returns antifactor IIA activity to zero. This is a promising alternative to use of protamine.[176]
   2. **Recombinant platelet factor 4** neutralizes heparin by a polycationic-polyanionic interaction. It reverses heparin when given in a ratio of 3:1 to the dose of heparin.[177]
   3. A **heparin removal device** has been developed and used clinically in a few patients with protamine sensitivity. This system uses a double-lumen cannula placed in the right atrium and a venovenous circuit. This contains a pheresis chamber in which heparin binds to poly-L-lysine and is removed from the blood.[178,179]
   4. **Hexadimethrine** has been used on a compassionate basis in a few patients with protamine allergies but is not clinically available in the United States.[180]

5. A low-molecular-weight protamine preparation has been investigated in canine models and has been shown to be effective in neutralizing heparin without demonstrating any adverse hemodynamic responses caused by nonimmunologic mechanisms.[181]

J. Treatment of coagulopathy. A meticulous operation and routine use of antifibrinolytic drugs in a patient with no preexisting coagulation problem should result in minimal postoperative bleeding. However, a coagulopathy is present in all patients to varying degrees after CPB. Generally, the longer the duration of CPB and the greater the number of blood transfusions required on pump, the greater the coagulopathy. Furthermore, preoperative medications, especially the ubiquitous antiplatelet agents, have adverse effects on hemostasis.

1. Most groups treat coagulopathies in the operating room by the "shotgun approach." This entails the empiric administration of additional protamine and transfusion of platelets, fresh frozen plasma, and, occasionally, cryoprecipitate. However, it is best to prioritize these products based on suspicion of the hemostatic defect. For example, platelet transfusions should be given first to patients on aspirin or clopidogrel or with uremia; fresh frozen plasma should be considered first for patients on preoperative warfarin, with hepatic dysfunction, or when multiple transfusions are given on pump; and uremic patients might benefit from desmopressin (see Chapter 9).
2. Although these approaches will usually stem the "coagulopathic tide," it is more scientific and cost-effective to use point-of-care testing to assess the specific hemostatic defect and direct care accordingly. Systems are available to measure the PT, PTT, and platelet count, and several are capable of measuring platelet function as well.[114,182,183] Other tests, such as the thromboelastogram, can provide an assessment of the exact hemostatic defect, but this test is time-consuming and rarely used.
3. Further comments on the treatment of bleeding and specific coagulation defects associated with aspirin, clopidogrel, and the IIb/IIIa inhibitors are presented on pages 95–98.

IX. Anesthetic Considerations During Off-Pump Surgery (Box 4.2)[184]

A. Monitoring considerations

1. In contrast to on-pump surgery, off-pump surgery via a median sternotomy requires that the heart provide adequate systemic perfusion at all times. Hemodynamics may be compromised by positioning of the heart, myocardial ischemia, ventricular arrhythmias, bleeding, and valvular regurgitation.
2. To ideally monitor a patient for myocardial ischemia and dysfunction when the heart is positioned at unorthodox angles, more intense monitoring is required than for on-pump surgery. Swan-Ganz catheters that provide on-line continuous cardiac output and mixed venous oxygen saturation are essential. These will dictate whether volume infusion or pharmacologic management is indicated. Simply maintaining an adequate blood pressure and heart rate pharmacologically may not suffice and often will provide no premonitory indication that the heart is becoming ischemic and subject to precipitous deterioration into ventricular fibrillation.

Box 4.2 • Key Elements of Anesthetic Management for Off-Pump Surgery

1. Continuous cardiac output and mixed venous oxygen monitoring
2. Transesophageal echocardiography
3. Antifibrinolytic drugs (probably of benefit)
4. Low-level heparinization with ACT of 300 seconds
5. Short-acting anesthetic agents
6. Maintenance of systemic normothermia
7. Arrhythmia prophylaxis with lidocaine and magnesium
8. Availability of pacing capability
9. Maintenance of hemodynamics with fluid, α-agents, and inotropes
10. Patience and emotional support for the surgeon!

3. TEE is helpful in assessing for the development of regional wall motion abnormalities during construction of an anastomosis. The anesthesiologist should be well trained in TEE and must immediately communicate any problem to the surgeon. Steps can then be taken to resolve the problem, often with the placement of a shunt to improve flow. During vessel occlusion, TEE should assess for the acute development of regional LV dysfunction or acute MR during construction of left-sided grafts and for RV or inferior wall dysfunction during right-sided grafting. If regional wall motion abnormalities persist after the graft is completed, a technical problem with the anastomosis should be suspected. The midesophageal windows are best for assessing RV and LV function. The transgastric views are not helpful when the heart is elevated out of the chest.[33]

B. Anesthetic agents are similar to those used for on-pump surgery, although shorter-acting medications may be selected depending on plans for extubation. Although patients can be extubated in the operating room, a more common practice is to use propofol for sedation at the end of surgery and for several hours in the ICU before considering extubation.

C. Heparinization is essential during off-pump surgery because coagulation is still activated by release of tissue factor and activation of the extrinsic pathway. The requisite amounts of heparin and minimally acceptable ACT levels have not been delineated. Usually 2.5 mg/kg of heparin suffices to raise the ACT to a level of 300 seconds. There have been concerns about the prothrombotic tendency noted after off-pump coronary artery bypass (OPCAB), since the hemodilution, platelet dysfunction, and fibrinolysis associated with CPB may not be seen. This prothrombotic tendency may be related to procoagulant activity of platelets or the activation of fibrinogen and other acute-phase reactants that result from the surgery itself.[185–189] However, clinical evidence of these problems, primarily graft closure, has not been confirmed at ACTs greater than 300 seconds.[112]

D. Antifibrinolytic therapy has not been studied extensively for off-pump surgery, although limited studies of aprotinin and tranexamic acid have shown benefits in reducing bleeding.[71,72] Although the blood is not subject to contact activation in an

extracorporeal circuit, heparinization does induce fibrinolysis, and thus use of any of the antifibrinolytic agents may be beneficial. ε-aminocaproic acid has been used routinely for OPCABs at many centers.

E. Patient temperature tends to drift during open-chest procedures but should be maintained as close to normothermia as possible to prevent arrhythmias, bleeding, and subsequent shivering in the ICU. The ambient room temperature must be raised into the mid-70s°F and some form of warming blanket should be used. These include a sterile Bair Hugger and heat-emitting devices, such as the Arctic Sun temperature-controlling system.[190] All fluids must be warmed and a heated humidifier placed in the ventilatory circuit

F. Maintenance of hemodynamics. During cardiac positioning, the patient is placed in Trendelenburg position and the operating room table is rotated to the right. Deep pericardial sutures are placed to aid with retraction. Apical suction devices can also be used to rotate the heart cephalad and to the right. Central venous and pulmonary arterial pressures increase in the head-down position, and care must be taken not to administer too much fluid and increase these pressures even more. Transducer location may need to be adjusted to ensure accuracy. The possibility of producing cerebral edema should be kept in mind.

1. Magnesium and lidocaine should be given to increase the arrhythmic threshold.
2. Blood pressure should be maintained in the 120–140 mm Hg systolic range to optimize coronary perfusion, especially collateral flow. This can be done with some fluid administration but usually with liberal administration of α-agents.
3. Atrial pacing wires may be placed if there is a concern about bradycardia developing with heart positioning. Transesophageal pacing may be utilized. Induced bradycardia is not essential with the latest generation of stabilizing devices. However, tachycardia should be controlled. Ventricular pacing cables should be immediately available in case heart block develops.
4. Detection of ischemia can be difficult, since the monitor ECG and TEE images can be difficult to interpret in the translocated heart. A reduction in the SvO_2 is one of the first signs of the struggling heart. Intracoronary shunting or aortocoronary shunting during construction of an anastomosis ameliorates distal ischemia. This is more likely to be required during bypass of the distal right coronary artery, which compromises flow to the atrioventricular node and produces heart block. Upon the first suspicion of ventricular dysfunction, the surgeon should be informed immediately so that a shunt may be placed, if not done so prophylactically, to try to minimize ischemia.
5. If inotropic support is required, low-dose epinephrine is given first, followed by inamrinone or milrinone if more support is needed. In high-risk cases, such as severe left main disease, a prophylactic IABP may be helpful. [191] Unless there is a strong indication for OPCAB, such as severe comorbidities, immediate conversion to an on-pump procedure may be a wise decision if instability persists.

G. Blood loss can be insidious during OPCAB. Blood should be scavenged into a cell saver and retransfused to the patient. Not infrequently, about 1 L of blood is lost and scavenged during these operations.

H. Proximal anastomoses are usually performed last. The blood pressure should be lowered to about 80–90 mm Hg systolic for application of the side clamp to minimize the risk of aortic injury and atheroembolization. Induced hypotension may

increase the risk of renal dysfunction. Distal perfusion is compromised after a graft is sewn to the aorta until the clamp is removed, and the patient can become unstable at this time.

I. Protamine is given in a 1:1 ratio to heparin. Bleeding should be minimal if the anastomoses are hemostatic. Pacing wires should be placed on the atrium and ventricle, chest tubes are placed, and the chest is closed.

J. The patient may be extubated in the operating room but more commonly is maintained on a propofol drip for several hours in the ICU. When the patient is normothermic, hemodynamically stable, and not bleeding, the propofol is gradually weaned off, and standard criteria for respiratory weaning and extubation are followed. Most patients are extubated within a few hours.

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